BUREAU OF HYGIENE AND TROPICAL DISEASES

BULLETIN OF HYGIENE

Volume 34, No. 2 February, 1959

Vital Statistics and Epidemiology

ANDERS, W. & MEIER, E. Epidemiologische Jahresübersicht 1956 für das Bundesgebiet und West-Berlin. **[Epidemiological Review for 1956 of the German Federal Republic and West Berlin]** *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 172, Nos. 3/4, 211–41, 14 figs.

In this review a great deal of information is given of the experience of the most important notifiable infectious diseases in the German Federal Republic and West Berlin in 1956. This experience is compared with that of 1955 which has been published [this *Bulletin*, 1957, v. 32, (639)]. The diseases included are diphtheria, scarlet fever, typhoid fever, paratyphoid fever, bacterial food poisoning, dysentery and poliomyelitis. Descriptions with many tables, figures and maps give information about morbidity, mortality, seasonal incidence, geographical distribution and particular variations of increase or diminution of incidence in different states and cities. In most of these diseases the overall figures of incidence were lower in 1956 than in 1955, with the exceptions that the number of notifications of bacterial food poisoning increased in the Federal Republic from 3,735 in 1955 to 4,442 in 1956 and poliomyelitis which had a peak year of 9,517 cases in 1952 followed by a year of low incidence (2,242 cases) in 1953 has since then shown a progressive increase to 4,109 cases in 1956. *M. E. Delafield*

Communicable Diseases

For the bacteriology of these diseases see the Section on Bacteriology below. For those communicable diseases conventionally regarded as tropical, readers are referred to the TROPICAL DISEASES BULLETIN

INFECTIVE DISEASES

In this section the abstracts are arranged as far as possible in the following order: General; Diphtheria, Whooping Cough, Streptococcal Infections, Staphylococcal Infections, Measles, Mumps; Chickenpox, Smallpox; Influenza and other Respiratory Virus Infections, Pneumonia; Hepatitis, Mononucleosis; Meningitis, Poliomyelitis and other Enteric Virus Infections; Encephalitis; Enteric Fevers.

U.S. DEPT. OF HEALTH, EDUCATION, AND WELFARE. **Immunization Information for International Travel.** Prepared by the Epidemiology and Immunization Branch, Division of Foreign Quarantine of the Bureau of Medical Services. *Pub. Health Service Publication No. 384.* Revised June, 1958. 71 pp., 3 maps. Wash. 25: U.S. Govt. Printing Office. [$0.30.]

Although this booklet has been prepared primarily for the convenience of Americans travelling abroad, it contains a great deal of practical information which is of use to travellers everywhere who wish to know what international health regulations apply to them. A preface outlines briefly the background of the international sanitary regulations and this is followed by details of documents and immunizations required and the relevant procedures to be followed. The immunizations required are those in respect of smallpox, yellow fever and cholera. The next section outlines immunizations recommended and this includes in addition those for the typhoid group, tetanus, typhus, diphtheria, plague and poliomyelitis. The third section states where immunizations may be obtained in the United States and the fourth sets out the United States immunization requirements in detail.

The fifth section lists the countries in the 5 continents and their required and recommended immunizations;

an additional column shows those further recommended by the United States Public Health Services.

The sixth section contains a list of addresses of designated yellow fever vaccination centres in cities in the United States, the clinic hours, and the fee charged, if any.

The seventh section gives useful information on the importation or re-entry of pets (psittacine birds, dogs, cats and monkeys) into the United States.

The last 2 sections consist of maps showing yellow fever endemic areas in Africa and in South America, and a map of yellow fever receptive areas in the United States.

At the end of the booklet there are blank forms in which changes in immunization requirements and additional yellow fever vaccination centres may be inserted.

The fifth and sixth sections have been brought up to date to June 1958. *H. J. O'D. Burke-Gaffney*

RUIZ SANCHEZ, F., RUIZ SANCHEZ, A., ACEVES, R. & NARANJO GRANDA, E. **The Use of Sulfamethoxypyridazine (Kynex) in the Treatment of Infectious Diseases.** *Antibiotic Med.* New York. 1958, July, v. 5, No. 7, 437–44, 3 figs. [25 refs.]

Sulphamethoxypyridazine [this *Bulletin*, 1957, v. 32, 361] is absorbed readily from the gastro-intestinal tract and high and prolonged blood concentrations are rapidly achieved. An average blood concentration of 27·5 mgm./ml. is achieved between 3 and 9 hours after a single 3 gm. dose (presumably in the adult) and a concentration of 13·9 mgm./ml. is still present after 48 hours. The drug reaches the cerebrospinal fluid rapidly in concentrations about half that of the blood. In this study, 40 patients suffering from a variety of infections were treated and good results are claimed; the diseases include carbuncles, blepharitis, scarlet fever, gonorrhoea and others; from all 12 cases of "carbuncle" *Bacillus anthracis* was isolated and all 12 patients responded well to a daily dose of the drug of 1·5–3 gm. for 5–10 days. It is difficult to assess the effects in patients in other groups as very little detail is given. Toxic reactions included 1 case of vomiting and abdominal pain, 1 drug rash, and 1 reduced erythrocyte count. *A. B. Christie*

MACIEREWICZ, Maria, OZIEMSKA-ŁOZINSKA, Halina & TYRMAN, Jadwiga. Ocena bakteriologicznych metod rozpoznawania błonicy. [**Bacteriological Evaluation of Methods employed in diagnosing Diphtheria**] *Med. Dośw. i Mikrob.* Warsaw. 1958, v. 10, No. 2, 213–21. English summary.

An evaluation has been made of the efficacy of the methods officially prescribed in Poland for the bacteriological diagnosis of diphtheria. Nose and throat swabs were taken from 271 children at the time of admission to hospital for suspected diphtheria, and were examined by stained smears and by inoculation on Loeffler, Clauberg and Liebig media. Bacteriological examination gave positive results in 122 (68·54%) of 178 cases in which the diagnosis was confirmed clinically, and in 15 (16·13%) of 93 in which there was no clinical evidence of diphtheria. The maximum number of positive results could only be obtained by the use of all the methods. The results obtained by examination of smears could be confirmed by biochemical tests in only 75% of cases; the percentage of confirmations of positive results obtained with Loeffler, Clauberg and Liebig media were 94·4, 100 and 100 respectively, but the procedure took too long to be of assistance in the treatment of clinically atypical cases.

D. J. Bauer

GOLDSMITH, H. J., COWAN, M. A. & GOODER, E. **Familial Outbreak of Acute Glomerulonephritis due to Griffith Type-1** *Streptococcus. Lancet.* 1958, Sept. 27, 674–5.

A family, comprising father and mother and 9 children aged 1½–17 years, experienced a series of infections due to a type 1 haemolytic streptococcus over a period of 9 weeks. 3 of the children developed acute glomerulonephritis and 1 other child had albumin and red cells in her urine. The mother and the eldest child had arthritis, with a raised sedimentation rate. Sera from the 3 cases of nephritis and from the mother contained antibody to type 1 streptococci and only insignificant antibody to type 12. *R. E. O. Williams*

KESSLER, Althea D. & SCOTT, R. B. **Staphylococcal Infections in Young Infants. Report of an Outbreak in a Hospital Nursery.** *J. Dis. Children.* Chicago. 1958, Sept., v. 96, No. 3, 294–8. [25 refs.]

Between March and June 1957, 20 newborn infants in a maternity hospital (2% of the live births) developed pyogenic lesions. Despite the fact that most full-term infants were discharged from hospital after 3 days, most of the infections developed in hospital. Staphylococci were isolated from 20 infants' lesions, 13 being phage-type 52/42B/80/81 and 3 52/52A/80. All were resistant to penicillin, streptomycin and tetracycline. In May and June 8 mothers were admitted to hospital with breast abscesses, but they were not examined bacteriologically.

Examination of healthy infants in the nursery in May showed that all acquired staphylococci of the type isolated from the infected infants. Novobiocin (80 mgm. daily) was therefore given to all infants, but this did not eradicate nasal carriage or prevent 2 infants developing clinical lesions. Erythromycin (40 mgm. daily) was therefore substituted and this prevented the development of the carrier state.

Eight of the nursing personnel proved to be transient carriers of one or other of the 2 prevalent types of staphylococci. *R. E. O. Williams*

FLOREY, M. E., with the technical assistance of Vera UNGEHAUER. **Infections due to** *Staph. aureus* **in a General Hospital.** *Brit. Med. J.* 1958, Aug. 16, 403–6. [15 refs.]

Of 11,670 admissions to the wards of the New York Hospital, 446 (3·8%) were admitted for the treatment of an acute infection; the proportion due to staphylococci is unknown, but 17% of the cultures from infected lesions examined in the laboratory yielded *Staphylococcus aureus*. The proportion was twice as high in

material from infections in the surgical out-patient clinic.

Surveys for the incidence of infection were carried out personally in 3 different clinics. In the surgical out-patient clinic some 33% of all admissions had clinically manifest staphylococcal infections. The rate was 13% in a surgical in-patient clinic and 17% in a medical in-patient clinic.

Of 123 staphylococci from lesions "none was found to be resistant to all six antibiotics" tested; 33 were sensitive to penicillin, 59 to tetracyclines, 111 to chloramphenicol and 102 to erythromycin.

1 patient with staphylococcal infection died, but death could not be completely attributed to the infection. In most other cases the infection was not serious. [The whole tone of the paper seems to be to minimize the importance of staphylococcal infection.]

R. E. O. Williams

HENDREN, W. H. & HAGGERTY, R. J. **Staphylococcic Pneumonia in Infancy and Childhood. Analysis of Seventy-Five Cases.** *J. Amer. Med. Ass.* 1958, Sept. 6, v. 168, No. 1, 6–16, 13 figs. [18 refs.]

Staphylococcal pneumonia, in infants particularly, has been markedly increasing in incidence in recent years, and this is an analysis of 75 consecutive cases of this serious disease treated at the Children's Medical Centre, Boston, during the last 6½ years. The largest group (51%) was of infants 1–6 months of age, and the average age in the series was 15 months. In the majority there was no specific history of exposure to staphylococcal infection, although 20 (27%) had cutaneous staphylococcal infections, and 15 (20%) had a history of exposure to family respiratory or other infection such as mastitis in the mother.

In the early stages diagnosis may be difficult, since there may be no signs referable to the chest; in other cases there may be a minimal haziness in a lung field in the chest film, followed later by focal nodular, or lobular, or even lobar infiltrations; an additional sign of some diagnostic importance is the presence of air blebs or pneumatoceles, due to infiltration of air into the interstitial tissue from necrosis and perforation of the smaller bronchi. The staphylococci were penicillin-resistant in 40 of the 46 instances in which the organism was isolated.

Vigorous treatment was needed, including blood transfusions, prolonged treatment with chloramphenicol and erythromycin in combination, and closed-tube thoracic drainage for empyema and tension pneumothorax. Streptokinase-streptodornase (Varidase) instillations were employed in 12 patients with thick purulent or fibrinous pleural pus. There were 9 deaths in the series.

H. Stanley Banks

CALVY, G. L. & SCHUMACHER, L. R. **Ristocetin and the *Staphylococcus*. Observations of Effects and Side-Effects in Seventeen Cases of Staphylococcic Pneumonia.** *J. Amer. Med. Ass.* 1958, July 26, v. 167, No. 13, 1584–6.

During an 18-month period there was an outbreak of staphylococcal infection at the U.S. Naval Hospital, St. Albans, New York, which included 37 cases of pneumonia. The staphylococcus responsible was of phage type "52-42B-80/81" and was resistant to the usual antibiotics; 1 patient had received "18 combinations of 10 different agents" unsuccessfully. Ristocetin was used for the treatment of 17 of these cases of pneumonia, the dose being about 25 mgm./kgm. daily, divided into 2 or 4 individual doses given intravenously, and continued for 15 days. 11 patients responded to this and 6 required a larger dose, of whom 2 developed thrombocytopenia and 3 phlebitis. Blood counts are advisable every 2 days, and renal function must be known to be satisfactory. Beyond the fact that all these patients recovered, this brief paper contains little information about them, and none about the fate of the remaining cases of pneumonia treated in other ways.

L. P. Garrod

CABRERA, H. A., HIBBARD, Betty & PADOVAN, B. L. **Staphylococcal Enteritis.** *Amer. J. Clin. Path.* 1958, July, v. 30, No. 1, 25–7.

The stools of 458 patients with gastro-intestinal symptoms from which no *Salmonella, Shigella,* pathogenic fungi or protozoa were isolated were cultured on blood agar plates containing phenylethyl alcohol as a selective medium for staphylococci. Stools from 61 symptomless people acted as controls.

Of the test group 14% yielded coagulase-positive staphylococci. [There is no indication of the numbers isolated or that the cocci were visible in direct films.] 5 of these came from patients with pseudomembranous colitis. These 5 strains and the majority of the rest were resistant to penicillin, erythromycin and several other antibiotics. 14 strains from the test group were phage-typed and were of several different patterns.

The authors stress the importance of using media selective for staphylococci when examining stools from patients with enteritis. [This practice appears to be less common in America than in Britain where the use of media containing 10% NaCl is the standard practice.]

[See also this *Bulletin*, 1953, v. 28, 734; 1956, v. 31, 559.]

M. Patricia Jevons

SCHWABACHER, Herta & SALSBURY, A. J. **The Clinical Evaluation of Staphylococcal Anti-Alpha Haemolysin Titres in Patients' Sera.** *J. Clin. Path.* 1958, Sept., v. 11, No. 5, 417–20, 3 figs. [12 refs.]

Repeated tests for antistaphylolysin were made on the sera of 5 patients with staphylococcal infections. 1 patient, with chronic osteomyelitis, never had an antibody titre greater than 0·5 unit per ml. The other 4 (with bone, muscle or blood-stream infection) had maximum titres between 4 and 32 units per ml.; 1 patient died, but in 2 of the other 3 there seemed to be a close relationship between the antistaphylolysin titre and the clinical condition, the titre declining rapidly when the clinical state improved. [Unfortunately there is no indication, on the graphs illustrating these 2 patients' histories, of the number of determinations performed; the range in variation of the titre shown in the graphs was about 2-fold.] In general the antileucocidin titre corresponded well with the antihaemolysin.

R. E. O. Williams

CROSBY, E. L. **Prevention and Control of *Staphylococcus* Infections in Hospitals.** *Indust. Med. & Surgery.* Chicago. 1958, Aug., v. 27, No. 8, 393–5.

This note summarizes the recommendations of a report recently issued by the American Hospital Association. It reviews briefly the factors associated with hospitalization that increase a patient's risk of acquiring staphylococcal infection, especially factors such as corticosteroid treatment or diabetes, which increase susceptibility, and exposure to persons already infected with virulent strains.

All hospitals should establish Infection Committees, and indeed this may be made a requirement for the accreditation of a hospital. The Committee ought to discover the incidence of infection, to review the services and techniques concerned with the prevention of infection, and to arrange an educational programme for the staff. Ascertainment of infections developing after a patient's discharge is important and the method of "telephone survey" [this *Bulletin*, 1957, v. 32, 198] is commended. *R. E. O. Williams*

PAPP, Carola. Voie d'infection du virus de la rougeole. **[Route of Infection with Measles Virus]** Reprinted from *Arch. Françaises de Pediatrie.* 1957, v. 14, No. 10, 4 pp.

In this article Professor Papp outlines her highly original views on the pathogenesis of measles, including the evidence that the sole route of natural infection with measles is across the intact conjunctiva.

In 1926 when she was working both in a measles ward and in a childrens' general ward 200 to 300 metres apart, new cases of measles kept cropping up in the general ward. The explanation appeared to be that she herself was acting as a carrier of the measles virus in her upper respiratory passages for a few hours daily, during which time she transmitted the infection to children in the general ward. A child thus infected in the general ward could also act as a carrier of the virus in its upper respiratory tract for a few hours, and so transmit the infection to another child during this period. The two children, neither of whom had been in contact with an actual case of clinical measles, could then develop the symptoms of measles at the same time.

In 1937 Papp tried on several occasions to transmit measles infection across the mucous membranes of the upper respiratory tract, but did not succeed. In 1954 she proved by several experiments in children [this *Bulletin*, 1955, v. 30, 941] that infective material from acute cases of measles could be transmitted only across the conjunctiva, and that such infection could be prevented by instilling 1 drop of convalescent serum into each conjunctival sac within 15 hours after exposure to the infective material. The disease could also be prevented if children exposed to close contact with an acute case of measles wore sealed off spectacles.

The use of convalescent serum instilled in the eyes has given practically 100% successful results in the hands of several colleagues, notably J. RUSTI [this *Bulletin*, 1958, v. 33, 813]. So far there have been 175 successful results reported in the prophylaxis of measles, and 78 in the prophylaxis of chickenpox, 102 in that of mumps, and 12 in that of rubella by the same method with the appropriate convalescent serum. 2 prophylactic methods against epidemics in children are thus available—the use of convalescent serum in the eyes of immediate contacts, and the use of spectacles in children attending consultation clinics.

It is not yet exactly known how the virus passes from the conjunctiva into the blood stream. From the fact that the incubation period is 4 days shorter when virus material is injected directly into the blood stream (by means of 1/100 ml. of blood from a case of measles in the acute stage) it may be concluded that the virus takes 4 days to reach the blood stream from the conjunctiva. This is in line with general experience that convalescent serum, injected during the first 4 or 5 days of the incubation period, prevents the development of measles. It seems therefore a reasonable assumption that the particular virus particles which reach the conjunctiva multiply in some unknown site for 4 days before passing into the general circulation. Here they live and multiply (presumably in the white cells) for 9 or 10 days, after which time the clinical symptoms of measles appear, apparently as an allergic phenomenon [see this *Bulletin*, 1959, v. 34, 14]. In this way the virus reaches the saliva, and thence is spread in droplets to restart the cycle of infection.

H. Stanley Banks

REYNOLDS, Audrey H. & JOOS, H. A. **Eczema Vaccinatum.** *Pediatrics.* Springfield, Ill. 1958, Aug., v. 22, No. 2, 259–67, 3 figs. [17 refs.]

The authors give detailed reports on 2 cases, and a summary of 7 others. 2 of these patients died.

Emphasis is laid on the extreme susceptibility to vaccinia of the child with atopic eczema. Though most patients become infected from a recently vaccinated sibling, 1 of the fatal cases here recorded was infected in a paediatric ward. The present authors consider that no child with atopic eczema should be vaccinated, but they go so far as to recommend that no child should be vaccinated if any member of the family has "eczema or other skin disorder".

[Thus to deny healthy members of the family protection against smallpox should be unnecessary when adequate temporary separation can be achieved.]

The danger of any contact with vaccinia should be made quite plain at an early stage to all parents of eczematous children.

Full use should be made of hyperimmune vaccinial gamma globulin in prophylaxis and treatment.

J. Pickford Marsden

FUKUMI, H., MIZUTANI, H., NISHIKAWA, F., YAMAMOTO, M., OKUMA, M. & KURIYAMA, S. **Epidemiological Studies of A/Asia/1957 Type Influenza in a Nursery near Tokyo City.** *Japanese J. Med. Sci. & Biol.* 1958, Apr., v. 11, Nos. 1/2, 1–12, 11 figs.

An outbreak of Asian influenza in a nursery with 44 children and 25 adults was studied by clinical and laboratory methods. Clinical evidence of infection

was observed in 26 children and 14 adults. The diagnosis of Asian influenza was confirmed by serological tests in all but 2 of the children and in 7 of the 14 adults. No antibody rises were observed in any of the children or adults without symptoms of influenza. 3 virus strains isolated from children's throat washings were identified as Asian influenza virus by haemagglutination-inhibition. *H. G. Pereira*

ROBERTSON, L., CALEY, J. P. & MOORE, Janet. **Importance of *Staphylococcus aureus* in Pneumonia in the 1957 Epidemic of Influenza A.** *Lancet.* 1958, Aug. 2, 233–6, 3 figs.

A retrospective review was made of the 140 patients with pneumonia admitted to a hospital in Sheffield during the height of the influenza epidemic in September and October 1957.

Cultures of sputum and necropsy material from patients, the majority of whom must have had post-influenzal pneumonia, yielded *Staph. aureus* in 27%, pneumococci in 9% and *Haemophilus influenzae* in 4% of specimens. No significant organisms were isolated from 46% of specimens, possibly owing to antibiotic treatment of patients before admission.

The mortality rate was 47% in cases where staphylococci were isolated and 16% in cases from which this organism was absent. In the staphylococcal group 19 patients were previously healthy and 8 (42%) died as against 7 of 13 (54%) patients who had chronic bronchitis.

Strains from all 18 fatal cases were sensitive to erythromycin, 12 were sensitive to aureomycin, chloromycetin, penicillin and sulphonamides, 9 of these being isolated from patients who had been in hospital less than 1 day. The 6 strains resistant to these antibiotics were isolated from patients who had been in hospital longer than 2 days, and there was evidence that these and 7 other strains from non-fatal cases were acquired in hospital. Bacteriophage typing of 16 strains did not reveal a predominant type.

M. Patricia Jevons

PAREDES, L., CABEZAS, J., PINO, M., GILARDINO, J., DE PABLO, J. & VALENZUELA, E. Bacteriología de las complicaciones broncopulmonares de la influenza. [**The Bacteriology of Pulmonary Complications in Influenza**] *Rev. Med. Chile.* 1958, May, v. 86, No. 5, 292–308, 5 graphs. [80 refs.]

This is a study of the bacteriology of pulmonary complications in 420 influenza patients admitted to the J. J. Aguirre Hospital in Chile during the winter (July–August) of 1957. Diagnosis was on a clinical basis in most cases, confirmation by virus isolation being carried out only in some. The complications studied were lobar pneumonia, bronchopneumonia, pleuropneumonia, pulmonary abscesses, pleural empyema and ill-defined pulmonary conditions. From 35 cases material was also obtained post mortem. Besides direct smear examinations, cultures were made of sputum, naso-pharyngeal secretions and in some cases of the blood. Biochemical and *in vitro* antibiotic sensitivity tests were made on some strains isolated. In serious cases the result of direct sputum examination (Gram stain) was reported immediately as a help in treatment.

The bacteria most frequently met with were: *Streptococcus pneumoniae* (59·3%), *Staphylococcus aureus* (16·9%), *Klebsiella pneumoniae* (12·2%) and *Streptococcus pyogenes* (4·3%). Compared with a non-epidemic period (1956) there was a statistically significant increase in pulmonary conditions due to *Staphylococcus* and a decrease in those due to pneumococci. The changes in those due to *Klebsiella* and *Str. pyogenes* were not significant. Some commensals of the nasopharynx appear to have played a part in some of the bronchopulmonary complications.

Blood culture carried out in 80 cases gave positive results in 9, staphylococci being isolated in 4, *Str. pneumoniae* in 2, *Klebsiella* in 1, *Str. viridans* in 1 and *Escherichia coli* in 1.

Serial sputum examinations (3–6 samples) of 100 patients receiving antibiotics showed changes in the flora, in the sense of a decrease in sensitive and an increase in resistant species. Hospital cross-infection with resistant strains was also studied. This was confirmed through the 35 cases studied post mortem, which also showed the greater frequency in fatal cases of *Klebsiella* and staphylococci.

On the basis of a complete study of 139 strains of staphylococci and 86 of *Klebsiella*, it is recommended that where the pathogenicity of a staphylococcus is doubtful, tests should include those for alpha-haemolysin, coagulase and phosphatase, and, for *Klebsiella*, its virulence for experimental animals.

This study confirms the findings of a previous one by the Institute of Microbiology and Immunity of the University of Chile on the existence of a high proportion of resistant staphylococci and *Klebsiella*. Staphylococci being highly resistant to penicillin and streptomycin, erythromycin and chloramphenicol are the antibiotics of choice. Oleandomycin is less active than erythromycin, and the phenomenon of cross-resistance between these two drugs was noticed. *Klebsiella* was resistant to streptomycin and less so to tetracyclines, chloramphenicol being the most active.

Compared with the previous year, there was a simultaneous increase in the percentage of strains resistant to penicillin, streptomycin, chloramphenicol and the tetracycline group. *Emanuel Agius*

MCCARROLL, J. R. & KILBOURNE, E. D. **Immunization with Asian-Strain Influenza Vaccine. Equivalence of the Subcutaneous and Intradermal Routes.** *New England J. of Med.* 1958, Sept. 25, v. 259, No. 13, 618–21. [16 refs.]

The antigenicity of an Asian influenza vaccine was studied in a group of 362 hospital employees by measuring the haemagglutination-inhibition titres of sera obtained after different vaccination schedules. The vaccine contained 200 CCA units per ml. and was administered to random groups of subjects, either in single or in multiple doses, by the subcutaneous or intradermal routes. A volume of vaccine given in 2 doses spaced by 7 days gave rise to better responses

then the same volume given in a single dose. Approximately identical responses were observed after subcutaneous or intradermal vaccination, provided the same dose was used for each route. *H. G. Pereira*

HILLEMAN, M. R., GREENBERG, J. H., WAREFIELD, Mildred S., ANDERSON, Sally A. & GLABERE, R. R. **Second Field Evaluation of Bivalent Types 4 and 7 Adenovirus Vaccine.** *Arch. Intern Med.* 1958, Sept., v. 102, No. 3, 428–36, 2 figs. [19 refs.]

A commercial vaccine containing formalin-inactivated adenovirus types 4 and 7 was tested for antigenicity in guineapigs and human beings, and for efficacy in preventing acute respiratory disease in army recruits. On arrival at the post 2,471 recruits were given 1·5 cc. of vaccine intramuscularly and 5,767 were injected with a placebo. A sharp outbreak of acute respiratory disease occurred during and following the period of vaccination. The protective effect of the vaccine was estimated on the basis of hospital admission rates and in about 50% of the cases the clinical diagnosis was checked by laboratory tests including virus isolation, complement-fixation with adenovirus antigen and haemagglutination inhibition of influenza A-prime and B. Vaccination reduced the attack rate for total respiratory infections by 55%. An assessment based on the results of serological tests showed that vaccination reduced the adenovirus-specific attack rate by 90%. A correlation between the results of virus isolations and complement-fixation tests showed that the latter procedure is highly reliable for the diagnosis of adenovirus infections, even among vaccinated persons.

[See also this *Bulletin*, 1957, v. 32, 1133.]

H. G. Pereira

LEATHER, H. M. **Pneumonia among Africans in Uganda.** *Thorax.* 1958, Sept., v. 13, No. 3, 222–8, 2 figs.

This is a study of pneumonia in 52 patients admitted to Mulago Hospital, Kampala, between September 1955 and May 1956; 44 were males and 8 females, and their ages ranged from 10 to 65 but only 3 were over 50 years old. The pneumonia was segmental in 26, lobar in 22 and lobular in 4. Pneumococci were isolated in 34 and staphylococci in 3 in sputum, laryngeal swabs, blood or post mortem material. Of the 15 indeterminate cases, 9 were thought to be bacterial in origin although no pathogens were demonstrated, and 6 were considered non-bacterial; these 6 had a longer period of onset than the others and were thought to have aspiration pneumonia. 3 patients died, all moribund on admission, and 2 of the 3 were suffering from staphylococcal pneumonia. Patients with pneumococcal pneumonia had typical symptoms and physical signs, well marked leucocytosis, and responded rapidly to penicillin. *A. B. Christie*

EDWARDS, G. & FEAR, E. C. **Adult Chronic Bronchitis—Continuous Antibiotic Therapy.** *Brit. Med. J.* 1958, Oct. 25, 1010–12.

This paper reports an extension of the successful trial of the treatment of patients with chronic bronchitis by oxytetracycline during the 6 winter months [this *Bulletin*, 1958, v. 33, 101]. Of those previously treated, 14 alternate patients were treated with oxytetracycline for a further 12 months, and 15 received blank control material. In the treated group no relapses, and even some further improvement, was reported; in the control group 2 out of 15 were improved, but 11 had relapsed. In a second investigation 13 of the 24 original controls were given continuous treatment (without oxytetracycline) for 6 months, and then 6 were treated with oxytetracycline for the 6 winter months; of these 4 were improved, and 2 unchanged, whereas of the 7 who did not receive the drug 3 had relapsed, and 4 were unchanged. The details of the relapses are then discussed. No ill-effects were noted, and a significant drug resistance did not appear. The authors conclude that repeated courses of 0·5–1·0 gm. of the drug daily each winter is likely to be of great value to patients with chronic bronchitis subject to relapses. [In spite of the relatively small numbers dealt with, this a well-regulated and valuable trial.]

F. H. Young

ALTER, A. A. & MICHAEL, M., Jr. **Serum Hepatitis in a Group of Drug Addicts.** *New England J. of Med.* 1958, Aug. 21, v. 259, No. 8, 387–9, 1 fig.

Drug addiction among adolescents in New York is increasing, and heroin is being self-administered by intravenous injection. Transmission of malaria, tetanus, acute endocarditis, septicaemia and serum hepatitis has already been reported. This is an account of 9 heroin addicts, aged 16–21 years, who banded together to share their crude equipment for intravenous administration. As a result 7 of them developed jaundice. The source of the infection was apparently a late incomer to the gang who had been in hospital 1 year previously with hepatitis. The incubation period appeared to be 3–6 months, the clinical symptoms were mild in these instances, and the virus infection was probably that of serum hepatitis.

H. Stanley Banks

BRUMFITT, W. & O'GRADY, F. **Laboratory Diagnosis of Glandular Fever.** *Postgraduate Med. J.* 1958, Oct., v. 34, No. 396, 535–40, 2 figs. [32 refs.]

In the series of patients with glandular fever and their contacts studied here all were included who showed the typical disease with sore throat, headache, malaise and widespread lymphadenopathy or who developed an acute febrile illness in immediate association with such patients. In this way 54 cases were diagnosed on clinical or epidemiological grounds.

The wide variety of clinical manifestations of glandular fever and the non-specific nature of milder attacks make it impossible to diagnose the disease with any certainty on clinical grounds alone except in the most typical cases or during an epidemic. Lymphocytosis is a common and frequently early finding in the peripheral blood, but it is of no diagnostic value unless it can be shown to be of a certain minimum magnitude. The observations of BAYRD (*Med. Clin. N. America*, 1956, v. 40, 1091), who claimed that 50%

lymphocytosis was an invariable finding within the first 10 days, and of SHUBERT *et al.* [this *Bulletin*, 1954, v. 29, 1028], who could not confirm the findings of Bayrd but found a maximum lymphocytosis of 4,000 in all cases, could not be confirmed by the results of the present series of observations. Abnormal mononuclear cells in the peripheral blood, resembling those described by DOWNEY and MCKINLAY (*Arch. Intern. Med.*, 1923, v. 32, 82), may be found in a variety of conditions other than glandular fever but the maximum number is less. In the present series no patient with glandular fever had persistently less than 10% of abnormal mononuclear cells. It appears, therefore, that in both sero-positive and in sero-negative glandular fever more than 10% of the mononuclear cells show the abnormalities described by Downey and McKinlay, whereas in other conditions this number of cells is never seen. The diagnostic value of the absolute number of abnormal cells is less. In the present series 8 patients showed persistently less than 1,000 abnormal mononuclear cells per cmm. and of these only 2 had an absolute lymphocytosis in excess of 4,000. More than one type of Downey cell is usually present but in genuine cases one type predominates. In all the cases studied the maximum number of abnormal mononuclear cells appeared within a week of the onset of symptoms.

It must be accepted that cases of glandular fever occur in which, despite careful and repeated study, sheep cell agglutinating antibody cannot be demonstrated. Shubert claims that sero-negative cases show rashes, while sero-positive cases do not. No rashes were found in sero-positive cases in the present series, hence the presence or absence of a rash may help in deciding if a case is likely to be sero-positive. While it is true that a number of unrelated conditions may be positive even to a high titre to the Paul-Bunnell test. in all these conditions the antibody is of the Forssman type. Any antibody remaining after guinea-pig absorption, therefore, is of the type associated with glandular fever. The evidence suggests that in other conditions and in non-contact normal subjects antibody of the glandular fever type very rarely exceeds a titre of 1/56. Circulating antibody may be present for a short time only and may appear late in the disease or even only in convalescence.

In the cases studied here there was a close relationship between the maximal percentage of abnormal mononuclear cells and the maximal absorbed Paul-Bunnell titre.

The thymol turbidity test has been recommended as a useful adjunct in the diagnosis of glandular fever. In the present series only 7 out of 31 patients tested gave thymol turbidities of more than 4 units. It must therefore be considered as of limited diagnostic value.

Provided early and repeated examinations are undertaken, glandular fever can be diagnosed or excluded in the laboratory with some confidence. The important pathognomonic findings are the presence in the peripheral blood, usually within a week of the onset of symptoms, of 10% or more of cells of the Downey type. Sheep cell agglutinating antibodies may or may not appear, but antibody which is not absorbed by guinea-pig kidney is characteristic of glandular fever and a titre of 1/56 or more is diagnostic. High titres of glandular fever type sheep cell agglutinins occur only in association with large numbers of abnormal cells, but in certain cases of glandular fever sheep cell agglutinating antibodies may not appear even in the presence of many abnormal cells.

[The ox cell haemolysin test might have given some interesting results in these cases. See below.]

P. A. Clearkin

MIKKELSEN, W., TUPPER, C. J. & MURRAY, Jean. **The Ox Cell Hemolysin Test as a Diagnostic Procedure in Infectious Mononucleosis.** *J. Lab. & Clin. Med.* 1958, Oct., v. 52, No. 4, 648–52.

In 1935 BAILEY and RAFFEL (*J. Clin. Investigation*, 1935, v. 14, 228) first reported the presence of haemolysin for ox red blood cells in the serum of patients with infectious mononucleosis. The authors of this paper compared the results of this test with those obtained by the test for heterophile antibodies as usually carried out.

Complete medical histories and physical examinations were made of 183 patients with the presumptive diagnosis of infectious mononucleosis. Total and differential white cell counts were performed as a routine on each, and heterophile agglutination tests, including adsorption with guineapig kidney antigen and ox cell haemolysin tests, were performed on each of 208 serum specimens obtained from the patients.

Ox cell haemolysin test. Serum was inactivated by heating at 56°C. for 30 minutes. To each of 10 test-tubes was added 0·5 ml. of 0·85% sodium chloride containing 0·1 gm. magnesium sulphate per litre. 0·5 ml. of inactivated serum was then added to the first tube and serial dilutions made; 0·5 ml. of complement solution was added to each tube, followed by 0·5 ml. of a 2% suspension of beef red blood cells. Commercial dried complement appears to have been used, diluted 1 in 15. After thorough mixing, tubes were placed in a water bath at 37°C. for 15 minutes, centrifuged at 2,000 r.p.m. for 2 minutes and read in comparison with a 50% haemolysin standard. This was prepared by adding 0·5 ml. of complement solution and 0·5 ml. of 2% suspension of beef red blood cells to 2 ml. of distilled water. The end point titre was the dilution in the tube reading closest to the standard. No difficulty was experienced with beef red blood cells up to 2 weeks of age. Ox cell haemolysin titre of 1 to 48 or less was considered negative, 1 to 96 to 1 to 384 suspicious and 1 to 796 or greater positive. Results of the 2 procedures were carefully compared in 72 patients with confirmed infectious mononucleosis and in 92 patients suffering from other complaints. In the former group the overall incidence of positive results with the ox cell haemolysin test was greater (75%) than with the heterophile agglutination test (52%). In no case was the heterophile agglutination test positive when the haemolysin test was negative. Moreover, the haemolysin test was more frequently positive in the first and second weeks of illness than the heterophile agglutination test.

Technically the ox cell haemolysin test has proved to be simpler and faster and less expensive to perform

than the heterophile agglutination test, and it can be completed in approximately 30 minutes after inactivation. It is suggested that greater diagnostic assistance will be obtained by performing both tests rather than either alone. *P. A. Clearkin*

VANDEPUTTE, M. & BERVOETS, W. Immunologie de la poliomyélite en milieu rural congolais. [**Immunology of Poliomyelitis in a Rural Area of the Belgian Congo**] *Ann. Soc. Belge de Méd. Trop.* 1958, Apr. 30, v. 38, No. 2, 219–23, 1 map & 1 chart.

Samples of serum were obtained from people of different ages living in a rural area in the Belgian Congo and tested for neutralizing antibodies against all 3 types of poliovirus. Antibodies appear at an early age, being present to all 3 types in 90% of the sample studied between 6 and 10 years. Antibodies to 1 type were present in almost all children by 3 years of age. The numbers studied were rather small, but it seems as if Type 1 antibodies appear rather more slowly than Type 2. *A. J. Beale*

VAN ERP, T. **An Epidemic of Poliomyelitis in South Sumatra.** *Trop. & Geograph. Med.* Amsterdam. 1958, June, v. 10, No. 2, 154–6, 1 fig.

In 1953 and 1956 there were 8 and 25 cases of paralytic poliomyelitis respectively among employees of the Royal Dutch Shell Company in Pladju, Sumatra. There is more interest in medical facilities among staff members than among labourers. About 30% of the cases were in the families of staff members who accounted for only 5% of the population. There was 1 adult case but the great majority of the patients were born after 1953 and in fact only 1 had been in Pladju for the 1953 outbreak. It is noted that despite the high sanitary standard achieved in this community the pattern of poliomyelitis followed that of underdeveloped countries. *A. J. Beale*

KITAMURA, I. **Some Observations on the Outbreak of Encephalomeningomyelitis encountered in Ehime-Syuso Area through Twenty-Eight Hospitalized Patients (1956).** *Acta Med. Okayama.* 1957, Dec., v. 11, No. 4, 327–37, 1 fig. [28 refs.]

An outbreak of poliomyelitis in the Ehime-Syuso area of Japan in 1956 is described in picturesque English. In all there were 78 cases, 45 paralytic and 33 non-paralytic. In a group of 28 patients seen at one hospital 16 complained of lethargy, in many cases amounting to drowsiness. One patient had a skin eruption but no details are given. Attempts were made to isolate a virus by inoculation of HeLa cell cultures with faeces obtained from 13 patients. 7 viruses were isolated, 4 were Type 1 poliovirus and 3 remained unidentified. 2 of the patients yielding poliovirus were paralysed, as was 1 who yielded an untypable agent. It was concluded that the epidemic was probably due to Type 1 poliovirus. *A. J. Beale*

MELNICK, J. L. **The Use of a Portable Tissue Culture Laboratory in a Field Study of Tropical Poliomyelitis.** *Amer. J. Pub. Health.* 1958, Sept., v. 48, No. 9, 1170–80, 3 figs.

The first recognized poliomyelitis epidemic in British Guiana occurred at the end of 1956 and beginning of 1957. There had been a falling infant mortality rate since 1920 which declined to around 80 in the past 5 years. The outbreak was one of infantile paralysis with the highest incidence in the children aged 0–4 years. The disease was mild and the overall attack rate 14 per 100,000. During March 1957 Melnick spent 1 week in the area with a mobile virus laboratory equipped with monkey kidney tissue cultures, specific diagnostic antisera, and complement-fixing antigens. He was able to establish that the epidemic was due to Type 1 poliovirus although Type 2 probably caused some cases (12 isolations were made from patients—7 Type 1, 2 Type 2 and 3 untypable with polio antisera whereas 200 healthy persons yielded 2 Type 1 viruses). 7 strains were typed by the complement-fixation test, 5 satisfactorily but 2 gave cross-reactions (a Type 1 with Type 3 and a Type 2 with both other Types). Complement-fixation tests on single sera gave evidence of Type 1 virus infection. 20 out of 38 cases giving fixation, against 2 out of 29 control healthy children. A serological survey of the population was also carried out. It was found that neutralizing antibodies to all 3 types appeared early in life and persisted, but that the peak titres were found about 5–9 years of age with a decline thereafter. Complement-fixation tests indicated also that infection with poliomyelitis viruses was prevalent among the younger children.

Dr. Melnick was asked whether killed poliovaccine was advisable for the population. He considered it unnecessary during the epidemic, because (a) it is no good in the face of an epidemic, (b) poliovirus was well seeded throughout the community, (c) it would be too costly for a country with more serious health problems. He advised, however, that a programme of poliovaccination will be required shortly as the standard of living, judged by the fall in the infantile mortality rate, continues to rise.

[This investigation shows how much a determined and enthusiastic investigator can achieve in helping the public health authorities in an underdeveloped area.] *A. J. Beale*

FOX, J. P., GELFAND, H. M., LEBLANC, Dorothy R. & ROWAN, D. F. **The Influence of Natural and Artificially Induced Immunity on Alimentary Infections with Polioviruses.** *Amer. J. Pub. Health.* 1958, Sept., v. 48, No. 9, 1181–92. [12 refs.]

In this interesting paper the authors bring their account of the study of poliovirus infections among families in Louisiana up to date [FOX *et al.*, this *Bulletin*, 1958, v. 33, 931; GELFAND *et al.*, *ibid.*, 931; GELFAND *et al.*, *ibid.*, 1957, v. 32, 1031]. All the remaining non-immune children in the study were given poliovaccine in 1956 and a booster dose in January, 1957. The response to a 2-dose primary course

was very poor for children previously without antibodies to any type of poliovirus. 36%, 26% and 60% failed to achieve antibody titres of 1 : 2 against Type 1, 2 and 3 virus respectively, whereas the percentages for those with heterologous antibodies were 10%, 8% and 18%. This vaccine was a commercially available batch, but for the booster injections a highly potent vaccine was selected by the Division of Biologic Standards of the National Institutes of Health. The response of those with heterologous antibodies prior to the primary course was now good, 88%, 80% and 49% having titres over 1/100 to Types 1, 2 and 3 respectively. On the other hand the poor response of the triple negative children was maintained, 23% failing to respond to Type 1 and 50% to Type 3. All produced some antibodies to Type 2.

The main purpose of this enquiry was to determine the effect of immunization on the incidence of natural poliovirus infection in the study households. In 1956 (after the primary poliovaccination) the number of incidents of household infections was about the same as in 1955 but far fewer infections were noted in 1957. This reduction could not, however, be ascribed to poliovaccination.

The infection rates for children under 15 were 92% for unvaccinated, 91% after a primary course and 83% after a booster dose. On the other hand naturally acquired antibodies did seem to reduce the likelihood of alimentary re-infection, the rate being 14% for children under 15. Not only do vaccinated children become infected with poliovirus, they also act as vehicles of intra-family spread of virus.

It is concluded that Salk vaccination does not create a barrier to the spread of poliovirus in the community. Evidence is reviewed that naturally acquired immunity and that following attenuated virus infection does prevent alimentary as well as paralytic infections. "It would, therefore, seem safe to predict that, when the basic safety of live-virus vaccines is accepted, their widespread use would create the immunologic barrier to virus spread which some now attribute (we think unjustifiably) to use of the Salk vaccine."

A. J. Beale

PETRILLA, A. **The Results of Intracutaneous Poliomyelitis Vaccination in Hungary, 1957.** *Acta Microbiologica.* Budapest. 1958, v. 5, No. 3, 297–309, 6 figs. [10 refs.]

In 1957 Hungary experienced its worst outbreak of poliomyelitis. There were nearly double the highest number of cases that had ever been reported previously, the attack rate being 23·8 per 100,000 population. The death rate was 6·1%. The outbreak was due mainly to Type 1 poliovirus which accounted for 46 out of the 53 strains of virus that were isolated. The epidemic started in May, which is considerably earlier than had previously been found with poliomyelitis in Hungary. In July a campaign of vaccination with Salk type poliovaccine obtained from North America was instituted. Vaccine was administered to children who were born in 1951 or later. Two 0·1 ml. doses of vaccine were given intradermally with a month's interval between them. 76% of the children under 6 years of age had received 2 doses by the end of September, and by the end of the year the proportion had risen to 80%. About 270,000 children over 6 years of age also received vaccine.

The vaccine was administered at the peak of the epidemic and it was not possible to inaugurate a controlled trial of its efficacy. Some attempt was made, however, to measure the effect of the vaccine, and it was concluded for the following reasons that it had an effect in preventing cases of poliomyelitis.

1. Although the epidemic far exceeded all those previously experienced in Hungary, the incidence during the last 3 months of the year was less in 1957 than in previous years. Similarly, the epidemic in Hungary declined earlier than the similar epidemic which occurred in 1957 in Rumania where no poliovaccine was employed.

2. Since most of the poliovaccine was administered to children under 6 years of age and considerably less to children over 6 years, the children under 6 years of age can be considered as vaccinated and those over 6 years as controls. In previous epidemics and in the early part of the 1957 outbreak the ratio of patients over 6 to those under 6 varied from 1 : 8 to 1 : 6, but in the latter part of 1957 after the inauguration of the vaccine programme the ratio fell to about 1 : 3.

3. An additional comparison was made between the experiences of the children under 6 years of age who were vaccinated and those who were not. In the country districts during the last 3 months of 1957 the incidence of paralytic poliomyelitis among those who refused vaccine was 26 per 100,000 and for those who were vaccinated it was 5 per 100,000.

Despite the admitted limitations of the methods of assessment it is concluded that 2 intradermal doses of poliovaccine were effective in preventing many cases of poliomyelitis. *A. J. Beale*

MARTINS DA SILVA, M. Respuesta a la infección con virus atenuado de poliomielitis durante el período neonatal y la primera infancia. [**The Response to Controlled Infection by Attenuated Poliomyelitis Virus in the Neonatal Period and Early Infancy**] *Bol. Oficina Sanitaria Panamericana.* 1958, Oct., v. 45, No. 4, 281–6, 6 figs.

The English summary appended to the paper is as follows:—

"A total of 138 pregnant women were vaccinated with Salk vaccine given intradermally or subcutaneously and 25 infants born of these mothers were given orally type 1 attenuated poliovirus (SM strain) before the age of six months.

"It was observed that: a) intradermal inoculation elicited as good an antibody response as the larger subcutaneous dose in those subjects whose antibody titres were measurable before and after vaccination; b) cord blood antibody titers were equal to or within one tube difference (within the error of the method) of maternal titer at delivery in over 85% of the instances where such comparisons could be made; c) no significant untoward reactions were observed in the infants fed the attenuated virus.

"It seems that vaccination with the live poliovirus vaccine is possible and adequate in the newborn period although titers obtained are lower than those attained at a later age. With the generalized use of Salk vaccine in pregnant women high titers of poliomyelitis antibodies are transferred to the baby at the time of delivery. We have observed that the proportion of pregnant women with naturally occurring poliomyelitis antibody titers equal to or greater than 1 : 1024 was increased from 10 per cent to about 44 per cent after two injections of Salk vaccine before delivery. The only baby in our series with an extremely high serum titer at birth (1 : 4096 or higher) failed to respond to the vaccine given on the fourth day of life.

"In an immunization program against poliomyelitis with the live poliovirus vaccine it would appear desirable to start vaccination as early in life as possible. If infection with the attenuated poliovirus and the resulting active immunity could be induced during the declining phase of passive antibodies, uninterrupted protection against the disease would be offered from the moment of birth. The newborn period would logically offer the best opportunity for such a vaccination program since it is the first time the baby comes under medical supervision and since almost all births (at least in the United States) occur in hospitals."

STEVENSON, W. J. **An Aspect of Salk Vaccination in Adult Women.** *Med. J. Australia.* 1958, Sept. 6, v. 2, No. 10, 325–6.

In June, 1956, in Victoria, Australia, there was a suspicion that inoculation with poliovaccine caused a delay in the onset of menstruation in women. This supposition appeared to be supported by the results of a questionnaire circulated to nurses before poliovaccination. It took a carefully controlled trial with a placebo substance as well as poliovaccine to demonstrate that in fact the vaccine was without effect upon the menstrual cycle. *A. J. Beale*

CHIN, T. D. Y., LEHAN, P. H., RUBIN, H., DOTO, Irene L., HEEREN, R. H., WENNER, H. A. & FURCOLOW, M. L. **Epidemiological Studies of Aseptic Meningitis caused by Coxsackie Virus B5.** *Amer. J. Pub. Health.* 1958, Sept., v. 48, No. 9, 1193–1200, 3 figs. [13 refs.]

An account is given of an extensive outbreak of non-bacterial meningitis occurring in Iowa in the summer of 1956. The outbreak was shown to be due to Coxsackie B5 virus which was isolated from 75% of patients with the disease and from 71% of those with minor febrile illness. Faeces was the best source of virus, but it was also recovered from throat swabs and the cerebrospinal fluid. All but 6 persons excreting Coxsackie B virus developed antibodies during convalescence. The attack rate was highest in children under 10 years and was equal for both sexes. Secondary cases in families were frequent, especially among young children. Based on a survey of 1,542 individuals in 404 households the overall incidence was estimated at 8%. *A. J. Beale*

HOSIER, D. M. & NEWTON, W. A., Jr. **Serious Coxsackie Infection in Infants and Children. Myocarditis, Meningoencephalitis, and Hepatitis.** *J. Dis. Children.* Chicago. 1958, Sept., v. 96, No. 3, 251–67, 13 figs. [15 refs.]

This paper contains a review of the 10 previously recorded fatal cases of Coxsackie B myocarditis and adds 2 more proven cases and a possible case. Most of the previous cases have occurred during outbreaks in maternity homes or when Coxsackie B virus has been causing disease (non-bacterial meningitis or Bornholm disease) in the community, but when these cases were discovered there was no such evidence of Coxsackie B virus infection. Both cases are described in detail; the first patient was 7 weeks old and presented with heart failure and died after a 10-day illness. Coxsackie B4 virus was isolated from the myocardium which showed extensive necrosis. The second patient was 8 days old, with jaundice, heart failure and tendency to bleed. There were necrotic and inflammatory lesions in the heart, liver (focal necrosis and haemorrhage), meninges and lung. Coxsackie B4 virus was recovered from heart, liver, kidney and lung. Unfortunately, these had been stored in one vessel and the titres 7 months later were heart $10^{-3 \cdot 66}$, kidney $10^{-1 \cdot 5}$, liver undiluted positive only, lung negative. Another fatal case of meningoencephalitis and focal hepatic necrosis in a boy aged 6 days is described. No virus studies were performed, but since the mother developed pleurodynia the day after delivery Coxsackie B infection is thought to be a possible cause.

Finally a case of heart failure with recovery in a boy aged 5 years is described. The illness started with an upper respiratory infection 5 weeks before he was seen by the authors. He was excreting Coxsackie B2 virus in the stools and serum taken 7 and 14 days after admission (6 and 7 weeks after probable onset) showed a rise in antibody titre to Coxsackie B4.

[See also this *Bulletin*, 1959, v. 34, Jan.]

A. J. Beale

UTZ, J. P. & SHELOKOV, A. I. **Coxsackie B Virus Infection. Presence of Virus in Blood, Urine and Cerebrospinal Fluid.** *J. Amer. Med. Ass.* 1958, Sept. 20, v. 168, No. 3, 264–7, 1 fig. [18 refs.]

A biochemist who had been working with viruses (including Coxsackie B3) for about 4 years developed an illness characterized by fever, rigors, myalgia and headache. He had slight neck stiffness and 147 leucocytes per cmm. of cerebrospinal fluid. Coxsackie B3 virus was isolated from the blood, cerebrospinal fluid, throat, anus and urine. The virus was obtained from the blood on the second day of illness both in suckling mice and monkey kidney tissue cultures. The urine was concentrated before successful virus isolation was achieved, but the technical details are not given. It was estimated that about 10–20 virus particles were present per millilitre of urine. The virus may have been present in very low amounts in the blood and have been concentrated in the urine. Since the patient

showed some evidence of renal impairment (the excretion of phenolsulphonphthalein was delayed) it is thought possible that there might have been an active virus infection of the renal tubules. *A. J. Beale*

FLUGSRUD, L., ABRAHAMSEN, A. M. & LAHELLE, O. **An Outbreak of Aseptic Meningitis associated with a Virus related to ECHO Type 9.** *Acta Med. Scandinavica.* 1958, Sept. 25, v. 162, No. 2, 129–35. [17 refs.]

An epidemic of non-bacterial meningitis due to ECHO 9 virus in the village of Aandalsnes on the West coast of Norway in April 1957 is described. In a population of 2,000 it is estimated that there were 35 patients with meningitis and 45 with minor illnesses. 13 patients were studied including 2 from a neighbouring town and 1 technician in the virus laboratory. The technician probably acquired a laboratory infection which she transmitted to her husband. 2 of the 13 patients had a maculo-papular rash. ECHO 9 virus was isolated from 8 patients, from the cerebrospinal fluid in 5 instances, in human amnion cells. 6 out of 10 patients tested showed a rise in neutralizing antibodies and all had antibodies in the convalescent serum samples whereas by contrast 11 out of 19 patients without meningitis in the same hospital lacked antibodies. The ECHO 9 strains were not pathogenic for suckling mice and were antigenically prime variants (*i.e.* they were not neutralized—or only in low titre—by antiserum to the prototype ECHO 9 virus, but antiserum prepared from them neutralized them and also the prototype strain). 9 of the 13 patients studied were adults and 4 were children, but in the population at large children formed the bulk of the patients. Multiple cases in families were frequent. *A. J. Beale*

HIRAKI, K., DEMIYA, Y., KAGEYAMA, H. & KIYAMA, A. **The Therapeutic Effects of ACTH on Japanese B Encephalitis.** *Acta Med. Okayama.* 1958, Apr., v. 12, No. 1, 51–62, 8 charts.

The authors treated 7 patients suffering from Japanese B encephalitis with corticotrophin, the dose being 1·5 mgm./kgm. per day, decreasing every day for a total of 7 days' treatment. All patients were severely ill on admission, with marked disturbance of consciousness. In each case there was a dramatic response: temperature fell rapidly and the neurological and mental changes cleared more gradually. The authors quote an average mortality rate of 30–40% for the disease and felt that treatment with corticotrophin is an advance; they would welcome unbiased reports from other workers. *A. B. Christie*

MAROJA, R. C., SILVA, J. C. & DE FREITAS, E. N. Surto de febre tifóide na usina serro azul, Município de Palmares—Estado de Pernambuco. [**Outbreak of Typhoid Fever in a Rural Sugar Plant in Palmares, Pernambuco, Brazil**] *Rev. Serviço Especial de Saúde Pública.* Rio de Janeiro. 1957, Dec., v. 9, No. 2, 223–33, 7 figs. & 1 map. English summary.

The authors report an outbreak of typhoid in April 1957 at a rural sugar plant in the state of Pernambuco, Brazil.

The outbreak lasted for a month, but 9 new cases, the subject of this report, occurred within 1 week among a population of about 1,300 persons, many of whom were employed at the plant and housed nearby. 7 patients sent to Recife for treatment were Widal positive while blood culture from 2 suspects at the plant was positive for *Salmonella typhi.* There was a heavy contamination of the drinking and washing water supplies; milk and other foodstuffs were excluded (except that the vegetables, etc. were washed with the contaminated water).

Examination of 1,085 samples of faeces from the population showed 4 positive for *Salm. typhi.*

The drainage of the plant and some of the houses went into a river, and there was a connexion between the river and the drinking supply source below this point. In addition a carrier was found in a mill above this point and faeces may have been washed into the river by heavy rains.

Among other preventive measures was the intradermal vaccination of 1,248 persons of all ages and both sexes. The management of the plant who owned the houses, promised to improve the water supply and sanitation. Although typhoid had occurred at this place before, the explosive onset of the 9 cases makes the authors think that the outbreak was water-borne.

[No details are given of the *total* number of cases which occurred, nor of the strength and dosage of the intradermal vaccine, nor about the 4 persons whose faeces were positive for *Salm. typhi.*] *W. K. Dunscombe*

SCHÄFER, W. Über die Dauer der Infektiosität von Salmonellosen. [**On the Duration of the Infectivity of *Salmonella*-Infections**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 172, Nos. 3/4, 272–81.

In the Federal Republic of Germany the law provides that patients who have had typhoid fever or paratyphoid fever shall not be regarded as free of infection until 3 negative bacteriological reports on specimens taken at intervals of 1 week have been obtained. If excretion of the organisms continues for a period of more than 10 weeks after fever has ceased the person concerned is put on the official list of long-term carriers. In Bavaria the regulations require that no person may be taken off this list until 10 negative reports have been obtained on specimens of faeces, urine and duodenal juice taken at intervals of 5–8 days. In Bavaria and certain other states of the republic these legal provisions do not, however, apply to salmonella infections other than those of typhoid and paratyphoid fevers.

In the investigation which is described in this paper the duration of faecal excretion of salmonella species in 313 patients who had suffered from enteritis was studied. Among the results of the enquiry it was found that excretion lasted for more than 4 weeks in 27·5% of patients, longer than 8 weeks in 10% and 6·7% of patients became long-term carriers according to the definition. It was also found in routine examinations of 5,300 healthy persons that 1·1% of

these were long-term salmonella carriers. There is a general discussion of the results and reference also to the findings of other workers with the recommendation that the extension of the existing law to long-term carriers of all salmonella infections should be considered. *M. E. Delafield*

De La Cruz, E. Epidemiología de la Salmonelosis en Costa Rica. I. Salmonelosis en porcinos. *Rev. Biologia Trop.* San José, Costa Rica. 1958, July, v. 6, No. 1, 27–35. [23 refs.] II. Salmonelas en carnes procesadas. *Ibid.*, 37–41. [13 refs.] [**Epidemiology of Salmonellosis in Costa Rica. I. Salmonellosis in Pigs. II. Salmonellosis in Processed Meats**]

The English summaries appended to the papers are as follows:—

(i) "The high incidence of *Salmonella* in liver, spleen, mesenteric lymph nodes, and feces of 150 apparently healthy pigs, for the local consumption of San José and surrounding areas is herewith discussed.

"The different serotypes that were isolated are reported with reference to their source of isolation and their frequency. Five of these serotypes had not yet been reported in hogs.

"For the first time in Costa Rica, the existence of 18 different serotypes is reported. The efficiency of tetrathionate broth using incubation periods of 24 to 48 hours is discussed.

"In a possible strain of *S. san diego* the presence of T 1 antigen of Kauffmann is reported."

(ii) "1. Two-hundred and fifty samples of processed meats from two of San José's meat processing establishments were examined bacteriologically.

"2. *Salmonella* was recovered from 20 (8%) of the samples.

"3. Twenty-two strains of *Salmonella* were isolated, corresponding to eight different serotypes, among which, *S. newport* and *S. reading* were most prevalent."

Voiculescu, M., Neuman, M., Elian, M., Horodniceanu, T., Russ, M., Vlad, R. & Dancu, J. Die Boyd-Ruhr. [*Shigella boydii* **Dysentery**] *Ztschr. f. Hyg. u. Infektionskr.* 1958, v. 145, No. 1, 34–41, 2 figs. [11 refs.]

This paper is a report on cases of dysentery due to *Shigella boydii* which occurred during an epidemic in 1957. This organism had not previously been isolated from any cases in the neighbourhood of Bucharest and had only once before been recorded in Rumania. The total number of patients with dysentery admitted to a hospital in Bucharest in August to October 1957 was 851 and of these infections 26 (3·05%) were due to *Sh. boydii*, 251 (29·4%) were Flexner dysentery, 64 (7·52%) were Sonne dysentery and 510 (60%) were clinical infections in which the causative organism was not determined. The clinical picture of the *Sh. boydii* infections, which ranged from that of a mild to a severe infection, is described with some account of the treatment with sulphonamides or with antibiotics. The techniques used in laboratory investigations are stated. With 1 exception all the isolated strains of *Sh. boydii* were found to be sensitive *in vitro* to a number of wide-spectrum antibiotics of which polymyxin and chloramphenicol were the most effective. It was also demonstrated that all but 1 of the strains of bacteria were of serotype 4 and phage type H, MS. The 1 exception was of serotype 2 and phage type Y_2. [A full report of the bacteriological investigations has been published elsewhere.] *M. E. Delafield*

TUBERCULOSIS

Woodruff, P. S. **Recent Trends in Tuberculosis in South Australia.** *Med. J. Australia.* 1958, Aug. 23, v. 2, No. 8, 245–52, 5 figs.

This is an epidemiological study of tuberculosis in South Australia (population 862,000). Age-specific death rates from the disease have been calculated for census years since 1911, which show that there has not only been a decrease in mortality but a progressive shift to older age-groups. Woodruff remarks, however, that the apparent change may represent only the passing of a generation of people susceptible to or subjected to this disease at every stage of their lives.

A similar study of death rates in females shows that the 1911 peak of tuberculosis mortality in young women has not moved to older groups and that fatal tuberculosis has not followed that generation through its life span. "Perhaps all the susceptibles were killed off in their early years." [No actual figures for either sex are given in the text, nor can they be found easily from the graphs which, however, show the trend clearly.]

There are 3,729 names in the central tuberculosis case register of South Australia (433 per 100,000), but this does not give an accurate estimate of the prevalence of this disease; it is deficient because of the omission of cases not yet notified and excessive because of the inclusion of patients whose names should have been removed but who have not bothered to obtain a certificate of clearance (which can be obtained from any doctor).

Since March 1952 all persons aged 14 years and over have been required to undergo X-ray examination. The response rate has been very high and information is available for 98% of the population in some areas, indicating a prevalence of previously unknown active tuberculosis in 0·089% (1 in 1,124 persons examined). Woodruff recommends that such surveys should be repeated every 3 years in South Australia.

Previously unrecognized tuberculosis is more than twice as common in males as in females, and its incidence in males increases with age. The overall discovery rate in males was 1 in 836 and in females 1 in 1,794.

There has been a slight but progressive decrease each year in the incidence of far-advanced disease notified—from 13% in 1953 to 9% in 1956. In spite of a 16% increase in the population in 6 years and increased

intensity in case-finding measures, the level of notifications has remained almost constant which indicates that the incidence of the disease is falling.

Examination of recent immigrants reveals almost double the incidence found in the general population. This is due to a much higher infection rate in the newcomers as judged by tuberculin surveys and to their habit of undertaking unduly hard and prolonged work.

There are about 3,000 persons of predominantly aboriginal stock of whom about 1,000 have been examined by X-ray and 1,261 tested with tuberculin. Tuberculosis appears to be more prevalent in this group than in the white population, but it is very rare among those living in semi-tribal conditions.

During the past 5 years 47,000 tuberculin tests were done (Mantoux 10 TU of OT) on army recruits, schoolchildren of all ages in rural areas and older schoolchildren in the city of Adelaide. Reactor rates in the last group fell from 8·5 to 4·1% for children born in Australia, but they were 39·4 and 20·4% in immigrant children. The rates in country children born in Australia fell from 5·2 to 2·5% and for immigrant country children from 18·6 to 8·1%. For national service recruits they fell from 21·2 to 15·3%, but the rate of fall was slowed up by the inclusion of immigrant youths after 1954. Details of reactor rates in aboriginals are given, showing differences according to location.

Woodruff draws attention to the need to replace the old-style sanatorium by the chest unit or hospital where relatively brief and intensive in-patient medical and surgical treatment may be given. He also stresses the need for the care of the respiratory cripple disabled by fibrosis, bronchitis and emphysema. A feature of recent years has been the more active treatment of children with established primary disease or recent infection. BCG vaccination is being most widely used in the teenage group in which primary disease appears much more likely to progress to destructive phthisis or dissemination than in the school child.

H. G. Calwell

MORAES, N. L. de A. É ainda grave o problema da tuberculose no Brasil? [**Is Tuberculosis Still a Serious Problem in Brazil?**] *Rev. Serviço Especial de Saúde Pública.* Rio de Janeiro. 1957, Dec., v. 9, No. 2, 215–22. English summary.

The author answers this question by pointing out that although the death rate per 100,000 in the Federal District and in São Paulo fell from 1946 to 1954, it is much higher than in other countries, and also while the number of new cases seen fell considerably in the same period, the number of persons dealt with by mass radiography was only 10% of the population. Further, many of those examined by X-ray were children, in whom the incidence is known to be low, and finally only 20% of the population live in the Federal District and the 20 state capitals, the condition of the remainder being quite unknown.

He then criticizes the work of the dispensaries, and points out that about 70% of the patients have either moderately or far advanced tuberculosis, thus showing that the dispensaries are not doing their proper work of detecting the early cases. The sanatoria too have 90% of long-stay, advanced cases; some are discharged sputum-positive, and the interrelation between the dispensaries and sanatoria is notoriously bad. Revision of the methods of production, distribution and administration of BCG is urgent; vaccination by the multiple puncture method should be practised, and the adverse influences of light and temperature on the vaccine should be made more generally known.

The author concludes by stating that in his opinion the tuberculosis problem in Brazil is not only grave but extremely so, and that the anti-tuberculosis campaign should be re-orientated.

[The author is being rather hard on his country as, owing to its immense size and rapidly growing population, the practice of preventive medicine cannot be an easy task.] *W. K. Dunscombe*

COCHRAN, J. B. & FLETCHER, W. B. **Radiographic and Tuberculin Survey in a Mental Hospital.** *Scottish Med. J.* Glasgow. 1958, Oct., v. 3, No. 10, 432–9, 3 figs. [16 refs.]

The Scottish hospital in which this survey was made in 1956 had 1,238 patients and 700 staff, of whom 90% and 98·6% respectively were examined.

X-ray examination revealed active pulmonary tuberculosis in 2 patients (0·18%). The prevalence of clinically significant tuberculosis (active and quiescent) was 1·1%. These findings were compared with those in a recent survey of a neighbouring rural area, and it was seen that the prevalence of active tuberculosis was similar but the amount of quiescent and arrested disease in the mental hospital patients was between 2 and 3 times higher than in the general rural population.

1 member of the staff was found to have active pulmonary tuberculosis but this was not a new discovery; 4 had quiescent and 14 had arrested disease.

The Heaf test was used in the tuberculin survey. The reactor rate in 1,109 patients was 72·2% and in 657 members of staff 83·7%. The higher reactor rate in the staff compared with the patients was found in all age-groups with sufficient numbers for comparison. The rate in patients permitted to visit the town was higher than in those confined to the hospital and it approximated to that of the staff.

There was evidence of waning sensitivity with age among the patients. The reactor rate rose sharply from 15 till 35 years and fell progressively thereafter.

In both patients and staff there was an overall preponderance of reactors in males compared with females but the present study provided no explanation of this.

In view of reports of the high incidence of pulmonary tuberculosis in patients in mental hospitals the incidence in this survey was surprisingly low. The large amount of quiescent and arrested disease found was, however, an indication of a high attack rate in the past.

If, as is likely, the maintenance of skin sensitivity to tuberculin is due to reinforcement of the original infection, the waning of sensitivity in the community studied here is evidence that the patients are not coming into contact with the tubercle bacillus. The

higher reactor rate among patients on parole and among the staff, most of whom lived outside the institution, supports this hypothesis.

In the group of male schizophrenic patients there was 3 times the amount of tuberculosis (all stages) found in the other males. This trend was reversed in females. Some workers have stated that the high rate of tuberculosis in mental hospitals is due to the special liability of schizophrenic patients to the disease. The reported relative insusceptibility of these patients to the common allergic diseases was not reflected by any unusual reaction to tuberculin in the group studied here. *H. G. Calwell*

PEPYS, J., BRUCE, R. A. & JAMES, D. G. **Multiple Puncture Depot Tuberculin (PPD) Cream Tests in Man.** *Tubercle.* 1958, Oct., v. 39, No. 5, 283–8.

This report describes reactions to tuberculin incorporated in various ointments and administered by HEAF's multiple puncture instrument.

PPD from the human type *Mycobacterium tuberculosis* was made into a solution containing 15 mgm./ml. as described and mixed with ointment of wood alcohols, liquid paraffin, emulsifying ointment and soft paraffin. Details of all these preparations are given. The best product was found to be anhydrous Eucerin made up to contain 5 mgm. of PPD per gm. This is referred to as depot PPD cream in the paper. Control preparations were made by using the same volume of aqueous solution as in the depot cream. None of these gave reactions.

The Mantoux tests were done with 1 and 10 TU of human type PPD and 100 TU of OT. Vaccination was done with fresh liquid Danish vaccine containing 0·75 mgm./ml. of semi-dried bacilli.

The Heaf tests with depot and control creams were read at 72 hours and later and interpreted by the usual criteria. The Mantoux tests were done with increasing doses of tuberculin up to 100 TU on the opposite arm. The criteria of a positive reaction was induration of 5 mm. or more at 72 hours.

Vaccination was done intracutaneously and the local reaction was regarded as normal if it did not appear until 10–14 days afterwards and then developed slowly and progressively with ulceration. The reaction was regarded as accelerated [Koch phenomenon] if inflammation developed within 3 days, began to subside within 7 days and left residual induration at 21 days.

32 student nurses aged 18 years and 489 factory workers were tested with the depot cream; 40% and 83% respectively reacted to the Mantoux test and 90% and 92% respectively to the depot cream.

59 miscellaneous out-patients were tested with liquid paraffin/lanolin cream and 73% reacted, including the 42% who reacted to the Mantoux test. 18 out of 29 subjects with sarcoidosis who did not react to the Mantoux test gave positive reactions when tested with the depot cream.

A group of infants and children numbering 49 and aged from 1 month to 14 years was tested solely with the depot cream and none reacted.

BCG vaccination was done on the 2 nurses and on 30 of the workers in the first series who did not react either to the Mantoux or to the depot cream test. The vaccination was performed 3 weeks after the depot cream test and another similar test was done on the other arm simultaneously with the vaccination. Both depot cream tests were positive 6 weeks after vaccination, which demonstrated tuberculin conversion and the persistence of the test material at the site of inoculation. There were no accelerated reactions to the BCG, and no reactions appeared at any time at any of the negative Mantoux test sites.

BCG vaccination was also done on 15 of the 19 nurses who, while not reacting to the Mantoux test, had reacted to the depot cream; 14 of these showed accelerated reactions to the BCG.

The depot PPD cream Eucerin has thus been shown to detect low degrees of tuberculin sensitivity and to persist locally so as to demonstrate subsequent tuberculin conversion. It could thus be used to provide a warning system for naturally occurring infection in non-reactors not vaccinated with BCG.

H. G. Calwell

VETERANS DEPT. OF MEDICINE & SURGERY. **Tuberculosis Laboratory Methods for the Veterans Administration-Armed Forces Cooperative Study on the Chemotherapy of Tuberculosis.** pp. iii + 34. 1958, June. Wash. 25, D.C., U.S.A.

The laboratory methods presented in this monograph were compiled to serve as a guide for the units in the cooperative study, and although most of them are already published, collected together in this form they make a valuable contribution not only to the bacteriological study of tuberculosis but to the safeguarding of laboratory personnel. The techniques described aim at reducing the risk of infection to the operator and emphasis is given where any procedure carries a special risk.

The first section is concerned with the microscopic detection of the tubercle bacillus but only the Ziehl-Neelsen stain is described. Section II is concerned with cultivation on ATS or Löwenstein-Jensen medium, and the treatment with caustic soda is described in detail for sputa, gastric contents and urine. The use of penicillin and Zephiran to control contamination and the testing for chromogenicity and catalase, are also described in this section.

Section III is concerned with drug sensitivity and in the method described the drugs are added to the egg medium before coagulation. This section contains 2 subsections, the first concerned with cycloserine and the second with pyrazinamide.

Section IV is particularly valuable for it has brought together the various characteristics and methods for distinguishing tubercle bacilli from other acid-fast bacilli. Section V is concerned with animal inoculation and the last section describes the various safety measures, including the use of safety hoods, ultraviolet radiation and germicides. An appendix gives formulae and descriptions of some non-standard methods.

Although alternative methods to some of those described may be considered preferable by some workers, this monograph is a valuable laboratory reference work. *S. R. M. Bushby*

BAUER, H. J. **The Observer Error in Multiple Interpretation of Photofluorograms.** *Acta Tuberculosea Scandinavica.* 1958, Suppl. 42, 90 pp. [59 refs.]

This is a most elaborate statistical investigation into the percentage of observer error in the interpretation of photofluorograms. It is of considerable importance that this should be known and if possible reduced; failure to recall a patient by under-reading the film will lead to a case being missed; over-reading is wasteful in time and money. 2,084,583 photofluorograms were taken on a standard apparatus on 70 × 70 mm. films under uniform conditions and read by 14 observers attached to the Stockholm mass radiography centre. 8 of these observers took part in the test. Single readings, independent dual readings, and re-reading of the same films by the same readers after an interval of 1–2 years were investigated. In a further trial, 100 test cases whose subsequent history was known were dispersed among 3,268 films and read by the interpreter in a similar manner. In addition the observers were tested on 101 films with artefacts. On the test series the correct average individual reading was 61%. This was increased to 76% after dual reading. There was a consistent percentage of error by individual observers in all tests, and error was regularly one of over- or under-reading by the same observer. The advantage of dual reading varied with the selection of the pairs of observers. The re-reading of the same films after 1–2 years produced an average variation of 32%.

The conclusion drawn was that although dual readings of various kinds had advantages, they were diminished unless all readers were specially trained and possibly tested after training. [This is a most careful investigation in which every effort has been made to exclude extraneous factors, and it can be received as an authoritative verdict on the subject.] *F. H. Young*

STEIN, H. & FREIMAN, Ida. **Phlyctenular Conjunctivitis in African Children.** *Arch. Dis. in Childhood.* 1958, Aug., v. 33, No. 170, 292–4, 1 fig. [10 refs.]

36 children aged 1–9 years, with phlyctenular conjunctivitis, seen in Baragwanath Hospital, Johannesburg, during 1 year were investigated. 22 showed active or healed tuberculous chest lesions by X-ray. Of 17 tested with tuberculin jelly patch test, 15 were positive. (It was considered inadvisable to test the remainder.)

This confirms the view that phlyctenular conjunctivitis is commonly associated with tuberculosis. It is not, however, analogous with erythema nodosum and its appearance bears no fixed relation to the onset of primary tuberculous allergy. *Cicely D. Williams*

LONG, E. R. **The Supporting Structure of Immunity in the Therapy of Tuberculosis.** *Amer. Rev. Tuberculosis.* 1958, Oct., v. 78, No. 4, 499–511. [26 refs.]

The founding of a lecture in honour of a man who is still alive is unusual, and this annual lecture is a recognition of the affection and respect in which Dr. J. BURNS AMBERSON is held. Dr. Long in his lecture reflected on the conclusions of all experienced pthisiologists—that certain patients get well in spite of every handicap, and others with every apparent advantage go down-hill steadily. He gives an account of methods of treatment in the past and present, and then touches on the factors which divide patients into the 2 groups, concluding that these are probably biochemical. [It is rather surprising that all except one of the references are to American literature.] The paper is well worth reading, especially by the younger generation. *F. H. Young*

FOX, W. **The Problem of Self-Administration of Drugs; with particular reference to Pulmonary Tuberculosis.** *Tubercle.* 1958, Oct., v. 39, No. 5, 269–74.

The failure by patients to take regularly drugs prescribed over long periods is common, and is becoming increasingly recognized. The author has investigated at the Madras Tuberculosis Chemotherapy Centre the magnitude of the problem as regards cachets containing PAS and isoniazid. By testing urine he found that during the first 6 months of treatment at home 20% of 58 patients defaulted on some occasions; this was reduced to 14% during the second 6 months. He examined the causes and came to the conclusion that the most important was indolence and lack of self-discipline. The results were worst in patients of low mentality and education. He does not consider that in Madras digestive disturbances are very important causes of failure. The percentage of defaulters in hospital was very low at 4% improving to 0·6% in the second 6 months. Unrelenting pressure and education by health visitors and nurses seems the only remedy. *F. H. Young*

DE ALEMQUER, M. **Severe Hypersensitivity Reaction to Para-Aminosalicylic Acid. Report of Two Cases and Review of the Literature.** *Amer. Rev. Tuberculosis.* 1958, Sept., v. 78, No. 3, 462–7. [Numerous refs.]

Sensitivity reactions to PAS are not infrequent, but they are rarely more than a problem for the doctor and an unpleasant episode for the patient, provided that the PAS is stopped at once. The author describes 2 cases in which the rarer dangerous reactions occurred. The features described in addition to the normal findings are: severe prostration, jaundice with hepatic enlargement, considerable pyrexia and haematological changes. The difficulty in deciding which drug is responsible when the patient is being treated by multiple drug therapy is emphasized. Both patients

recovered after the PAS was stopped. Cases previously described in the literature are discussed, and a very useful and comprehensive bibliography is appended. *F. H. Young*

LEWIS, D. O. **Drug Resistance in Pulmonary Tuberculosis treated with Calcium B-PAS.** *Tubercle.* 1958, Aug., v. 39, No. 4, 247–50.

Calcium benzamidosalicylate (Ca B-PAS) is claimed to be an effective alternative to PAS for combined drug therapy, but of 39 patients admitted to Sully Hospital during a period of 15 months and who had at least 2 months' therapy of Ca B-PAS with streptomycin and isoniazid, 20 yielded strains of tubercle bacilli which were fully or partially resistant to one or more of the drugs. This high incidence of resistant strains could be partly accounted for by the sensitivity of some of the strains before therapy being unknown and some of the patients not having had adequate therapy, but 7 of the cases were not open to these criticisms, and in 3 of these the bacilli became resistant during therapy and 2 others still had positive cultures after 6 months' treatment; 2 became sputum negative.

The author regards these results as evidence that the Ca B-PAS may not be a satisfactory alternative to PAS and he calculates that as the antituberculous activity of Ca B-PAS depends upon conversion *in vivo* to PAS, and as absorption is only about 60%, doses of 48 gm. and 28 gm. of Ca B-PAS are necessary for adequate cover of streptomycin and isoniazid, respectively, whereas the currently accepted dose is 14 gm.

The results of the trial by GIBSON and NAGLEY [this *Bulletin*, 1956, v. 31, 20] of Ca B-PAS are discussed and contrasted with those of trials with PAS, and in consequence serious doubts are raised about the claim for the drug being as effective as PAS.

S. R. M. Bushby

EVANDER, L. C., ROSE, N. R., BEUTNER, E. H., TASHIRO, K. & DOYLE, W. **Studies of the PAS Salt of Isoniazid in the Treatment of Tuberculosis.** *Amer. Rev. Tuberculosis.* 1958, Oct., v. 78, No. 4, 637–43.

This is a report on 19 patients treated with a chemical compound of PAS and isoniazid-isonicotinic hydrazide-*p*-amino salicylate (IP salt). Most of the patients had advanced disease, all had been previously treated without success with isoniazid and PAS, and all had positive sputa. In 16, the bacilli were resistant or partially resistant to isoniazid, in 16 they were resistant to PAS, and in 17 they were resistant or partially resistant to IP salt.

For 5 months the dosage was 200 mgm. 3 times a day, which was increased to 300 mgm. subsequently. 2 patients (both from the partially resistant group) had their sputum converted, but in none was any radiological improvement noted, and 2 died. This is a useful trial carried out under testing conditions, but it fails to confirm previous favourable reports.

F. H. Young

ROSS, R. R. **Use of Pyridoxine Hydrochloride to prevent Isoniazid Toxicity.** *J. Amer. Med. Ass.* 1958, Sept. 20, v. 168, No. 3, 273–5. [10 refs.]

Somewhat optimistic reports on the benefit received by tuberculous patients after large doses of isoniazid from the commencement of treatment, has made the assessment of the value of pyridoxine in preventing toxic effects important. This paper compares the incidence of these effects on 48 patients treated by 20 mgm. isoniazid per kgm. of body weight daily alone, and 62 patients who received pyridoxine 25 mgm. twice daily in addition. Larger doses of pyridoxine were adandoned as unnecessary. Nearly all toxic effects appeared within the first 24 weeks of treatment. At the end of 20 weeks' treatment 51% of the patients who were still in the series on isoniazid alone, and 25% of the pyridoxine group, had developed toxic manifestations. The difference was due solely to the appearance of neuritis in 14 patients in the isoniazid group, but only 1 in the isoniazid + pyridoxine group; in this case increase in the pyridoxine dosage caused the neuritis to disappear. Convulsions, psychosis, mental confusion and somnolence, transient dizziness and ataxia were rather commoner in the pyridoxine series. A table giving details is included.

F. H. Young

KIRSHNER, J. J. **Massive-Dose Isoniazid with Pyridoxine in Chronic Pulmonary Tuberculosis.** *Amer. Rev. Tuberculosis.* 1958, Sept., v. 78, No. 3, 474–7.

The use of very large doses of isoniazid with pyridoxine has been reported, especially by MIDDLEBROOK. The author of this paper decided to investigate this both from the point of view of reactions and clinical results. 34 patients were investigated, of whom 29 received at least 6 months' therapy, and in 5 treatment was abandoned because of toxicity. The usual daily dosage was 20 mgm. of isoniazid per kgm. of body weight combined with 1 mgm. of pyridoxine per kgm. Toxic effects included insomnia, transient tingling of fingers and toes, and giddiness. The last was severe in 3 patients, and mental confusion was noted in 2 patients. Temporary reduction of dosage usually produced improvement, and the original dose could be restored. 5 patients with emphysema became sufficiently dyspnoeic to call for discontinuation of the drugs. Peripheral neuropathy developed in only 1 patient, and in this case 2,800 mgm. daily were given in error. No abnormality of blood or liver function was noted.

Clinically and radiologically little benefit was obtained, except that 2 patients who had received no isoniazid previously progressed very favourably. The findings are similar to those noted by other workers—that if isoniazid has been used previously there is no advantage in giving very large doses. As most of the patients had been treated previously with the drug the investigation does not indicate whether massive doses given from the start are beneficial.

F. H. Young

RITCHIE, J. A., CAMPBELL, A. E. R., CUTHBERT, J. & BRUCE, L. G. **Treatment of Drug-Resistant Cases of Pulmonary Tuberculosis with Cycloserine and Pyrazinamide.** *Tubercle.* 1958, Oct., v. 39, No. 5, 289–95.

This is a small but careful investigation into the value, both absolute and comparative, of cycloserine and pyrazinamide in drug-resistant cases. In all, an additional drug to which the patients' bacilli were not resistant, or oxytetracycline if they were resistant to all the usual drugs, was given.

28 patients received cycloserine, 25 mgm. per kgm. body weight, and 35 were treated with pyrazinamide, 35 mgm. per kgm. body weight, maximum dose 2 gm. daily.

The toxic effects are set out in detail. In the case of cycloserine they were mainly mental depression, convulsions and other neurological symptoms. Recovery followed discontinuation of the drugs. Of the 35 patients treated with pyrazinamide, 7 developed evidence of liver damage within 3 months, and 1 died of this. In a few cases some improvement was thought to have occurred in the cycloserine group 9 months after termination of treatment, and it was readily acceptable to the patient. No definitive improvement was noted in the pyrazinamide group, and it made the patients feel below par.

In the authors' hands the bromsulphthalein liver test was found to be of little value. [This is a useful paper and should be read by anyone contemplating using these drugs.] *F. H. Young*

See also p. 135, MORROW & KANTOR, **Silicotuberculosis. Results of Medical and Combined Medical-Surgical Therapy.**

IRVINE, K. N. **Conversion Testing of Schoolchildren after B.C.G. Vaccination.** *Brit. Med. J.* 1958, Oct. 25, 1018–19.

The object of this investigation was to find out whether the post-vaccinal tuberculin conversion rate in 13-year-old schoolchildren vaccinated with Danish fresh BCG vaccine was high enough to warrant omitting the test in schoolchildren. The work was done in the Oxford Hospital Region, England, which embraces 6 counties and 3 county boroughs. Only non-contact children were included.

1 test only was used for pre-vaccinal and conversion testing; in 5 areas it was the Mantoux with 10 TU of PPD, and in 4 it was the Heaf test with PPD. The scheme was working smoothly in the school year 1956–57 during which 40 different batches of vaccine were used and valid conversion tests were done on 10,422 children. The results were:

	Mantoux test	Heaf test
Number vaccinated	6,917	4,867
Number validly tested	5,676	4,746
Number of reactors	5,471	4,647
Number of non-reactors	205	99
Conversion rate	96·4%	97·9%

It was concluded that post-vaccinal tuberculin testing of non-contact 13-year-old children is unnecessary. It is mentioned in a postscript to the paper that a similar trial is to be made in children vaccinated with Glaxo freeze-dried BCG. [The decision to discontinue routine post-vaccinal testing in school leavers in Northern Ireland was taken some 3 years ago on the same grounds as Irvine's.] *H. G. Calwell*

FREW, H. W. O. & RICHMOND, M. M. **Reversions after B.C.G. Vaccinations.** *Health Bull.* (Issued by the Chief M.O., Dept. of Health, Scotland.) 1958, Oct., v. 16, No. 4, 64–5.

In this attempt to estimate the rate of tuberculin reversion in children vaccinated with BCG 446 child contacts of patients with pulmonary tuberculosis were studied. These children, who had been non-reactors before vaccination, had all undergone post-vaccinal conversion. The vaccinations were done between May 1950 and March 1953, and a yearly follow-up was continued for 5 years.

Only 262 children completed the observation requirements; details of reversion rate are tabulated:

Age at vaccination	0–1 year		1–4 years		5–9 years		over 10 years	
	No.	reversions	No.	reversions	No.	reversions	No.	reversions
	72	1	82	11	83	17	25	9
Rate of Reversion	1·4%		13%		20%		36%	

The total number of children who completed the period of follow-up was 262, of whom 38 (14·1%) reverted.

Reversions were slightly more frequent in females but the difference was not statistically significant. As shown above the reversion rate increased steadily with age from 1·4% to 36%. [It would be interesting to know if the youngest infants were given a double dose of vaccine, as is often recommended.]

It was not found that there was an increased frequency of reversion during the observation period; the greatest number were found at the 3rd annual testing.

The children under observation were contacts normally living at home. Since vaccination the sputum of the index patients in contact with 234 of the children who completed the study was negative throughout the period. 28 children were in contact with sputum-positive patients and reversion occurred in only 3 of these children. The percentage of sputum-positive patients living with the children in the reversion and non-reversion groups showed no difference.

H. G. Calwell

CHAKRAVARTY, S. **Effect of BCG (*Bacillus* Calmette Guerin) Vaccination on the Occurrence of Tuberculosis among Student Nurses.** *Calcutta Med. J.* 1958, Aug., v. 55, No. 8, 258–64. [12 refs.]

Student nurses entering the school of nursing of Philadelphia General Hospital undergo a medical examination on entry (including X-ray examination of

the chest) and are examined by X-ray every 6 months thereafter. They are not assigned to the tuberculosis wards during their first 6 months and during the remaining 2½ years of training they spend all but 4 weeks in the general wards.

616 nurses entered the school during the period 1950–5 and were followed up for at least 2 years. All were Mantoux tested with 1 TU of OT. The reaction was examined at 48 hours and doubtful or non-reactors were tested again with 10 TU and vaccinated simultaneously with BCG. The local reactions to the 2nd Mantoux test and the vaccine were observed 48 hours later.

Of the 616 nurses 12·9% reacted to 1 TU, 4·3% to 10 TU and 10·1% gave a slight or doubtful reaction. The criteria of interpretation are not given but are stated to be those of ARONSON and MCGETTIGAN [this *Bulletin*, 1951, v. 26, 1075].

1 year after vaccination 328 nurses were tested with 10 TU and 61·6% were found to be reactors, 37·5 doubtful and 0·9% non-reactors. 2 years after vaccination 253 nurses were tested and the respective rates were 67·9%, 31·7% and 0·4%.

Of the 536 nurses who failed to react to 1 TU at entry 513 were vaccinated with BCG (including 26 reactors to 10 TU) and 23 refused vaccination.

3 nurses developed active pulmonary tuberculosis (5·9 per 1,000 vaccinated persons and 4·8 per 1,000 of the total enrolled). None of the 80 original reactors to 1 TU developed active tuberculosis. The 23 unvaccinated non-reactors did not develop active tuberculosis and only 4 (17·4%) became positive to 1 TU after 2 years.

[No explanation is given of what seems to the reviewer a most irrational practice, namely, vaccination on a single tuberculin test of only 1 TU which failed to detect sensitivity in 26 nurses who were in fact reactors to 10 TU and had therefore presumably been infected with virulent tubercle bacilli or vaccinated previously. No information is given about accelerated reaction to vaccination or the occurrence of tuberculosis in these 26 nurses.

Post-vaccinal sensitivity does not appear to have been studied until 1 year after vaccination and no information is given about the local reaction to the vaccine so that doubt about its potency is not resolved, and the fact that only 61·6% of those tested at 1 year reacted to 10 TU is almost conclusive evidence that the vaccination was most unsatisfactory. As the author remarks: "It would be difficult to try to evaluate the protective value of BCG vaccine in student nurses in this series".] *H. G. Calwell*

VENEREAL DISEASES

SCHNEEWEISS, U. & WEMMER, H. Vergleichende Untersuchungen zwischen Kapillar- und Venen-Trockenblutproben mit quantitativen Cardiolipin-Komplementbindungs- und Flockungsreaktionen auf Syphilis. [**Comparison between Capillary and Venous Blood in the Test for Syphilis by means of the Cardiolipin Flocculation Test and the Cardiolipin Complement-Fixation Reaction**] *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1957, Nov.–Dec., v. 3, No. 6, 379–90, 2 figs. [13 refs.]

For this investigation a micro-method was used which required only 0·2 ml. of blood and a blood sugar pipette was used to take the blood, both capillary and venous. Capillary blood was taken from the finger or ear, taking care not to exert pressure on the surrounding tissues. The finger may first be congested and then a deep puncture made. The first drop is discarded and the succeeding flow of blood allowed to run into the pipette up to the 0·2 ml. mark. The blood is then run into a Petri dish 6·0 cm. in diameter and spread evenly over the bottom, taking care to see that it does not touch the sides. It is then allowed to dry in the air, and the cover is replaced and closed with Elastoplast for transport. Venous blood is taken with a syringe and treated as capillary blood.

To prepare for testing, spread 0·3 ml. normal saline (0·9%) evenly over the dry blood smear, replace the cover and allow to stand at room temperature for 1 hour. After rocking the dish several times, remove 0·15 ml. of the solution for the cardiolipin flocculation test and to the remaining 0·15 ml. in the dish add 0·5 ml. veronal buffer solution, allow to stand 5 to 10 minutes, transfer to a small tube 8 by 80 mm. and inactivate for 15 minutes at 56°C. in a water bath. The chocolate-brown fluid is then centrifuged for 15 minutes at 4,000 revolutions, decanted and used for the cardiolipin complement-fixation test. The respective portions are then tested by the complement-fixation test and flocculation test in the usual manner.

The veronal buffer solution consists of a stock solution containing $MgCl_2$ $6H_2O$, 1·0 gm., $CaCl_2$ $2H_2O$, 0·2 gm., veronal 4·6 gm., dissolved in hot distilled water and sterilized by filtration and kept at 3 to 5°C. Add 3·0 gm. veronal-sodium, 2·52 gm $NaHCO_3$ and 83·8 gm. NaCl, cool to room temperature and make up to 2,000 ml. For use, add 1 part to 4 parts distilled water. *p*H should be 7·3–7·4. For preserving sheep's cells, take glucose 24·6 gm., sodium citrate 9·6 gm., sodium chloride 5·04 gm., distilled water to 1200 ml. Sterilize by filtration or by heating in the steamer for half an hour on 3 successive days. For use, equal parts of the solution and sheep's blood taken from the jugular vein are required. Keep in 20 ml. quantities at 3° to 5°C. After allowing 1 week for stabilization it may be used for 8 to 12 weeks.

In tests there was no significant difference between the results given by capillary and venous blood.

P. A. Clearkin

SCHNEEWEISS, U. Serologische Studien über die Haltbarkeit luftgetrockneter Blutproben. [**Serological Studies on the Duration of Activity of Dried Blood for Blood Tests**] *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1958, v. 2, No. 1, 76–91. [15 refs.]

2 series of experiments were carried out to ascertain the duration of activity of dried blood obtained from syphilitic rabbits, in cardiolipin flocculation and complement-fixation quantitative tests and the qualitative Meinicke test. The technique of drying the blood was described in a former publication [above] and is not repeated in this article. Control experiments were carried out with serum from infected rabbits kept in a cold chamber.

Results show that activity was well maintained in dried blood kept in a cold chamber where it maintained activity for 2 to 3 weeks and at room temperature where it was active after 7 days. Heat and moisture have a deleterious influence on dried blood. At 37°C. with air moisture of 20 to 30% activity may be maintained for 2 to 3 days but when the moisture is 80 to 90% survival is 24, or at the most, 48 hours. Under unfavourable climatic summer conditions in Berlin the upper limit was 5 days at room temperature.

P. A. Clearkin

SINNECKER, H. Zur Standardisierung und Kontrolle in der Luesserologie. I. Zur Frage der Standard-Trockenseren. [**Standardization and Control in the Serology of Syphilis. I. The Question of Standard Dried Sera**] *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1958, v. 2, No. 1, 63–75, 1 graph.

This paper considers not only the question of standard sera for control of the complement-fixation and cardiolipin flocculation tests but also the effect of variations in the other components. The author considers that cardiolipin antigen is the best available of the alcoholic extracts but that further work is required to attain the maximum reliability of serological tests for syphilis. Standardization of all components is necessary if discrepancies in the results, not only of different laboratories but even of the same laboratory, are to be avoided.

Positive syphilitic sera are required as controls and these were obtained from syphilitic patients, tested by the quantitative cardiolipin flocculation reaction and graded according to their titre into 3 groups, then frozen and dried *in vacuo*. Experiments showed that residual moisture must be reduced to at least 1·2%; a higher content resulted in a fall in titre and colloid-chemical changes. The optimum was 0·5%.

Antigen also requires to be standardized by titration with a number of sera as different batches may give different results. Fluid for dilution is also of importance as the electrolyte in NaCl solution varies often leading to variable results. When a buffer solution was used the *p*H fell within 1 month from 6·3 to 5·7. Control of the *p*H is therefore necessary. 3 buffer solutions were compared and all gave similar results in the Kolmer's qualitative test but the veronal buffer solution had the advantage of increasing the sensitivity of the Kolmer technique. Cleanliness of vessels and apparatus is essential as many substances may give false positive reactions. Automatic pipettes should be used.

Details of the technique, with standard preparations as supplied by the Institute for Epidemiology in Berlin, are given and it is considered that the reliability of serological tests can be increased by such standardization.

P. A. Clearkin

REYN, Alice & BENTZON, M. W. **Studies on the Effect of Variation of Concentration and Origin of Lecithin (Natural and Synthetic) in Cardiolipin Complement-Fixation Antigen.** *Brit. J. Venereal Dis.* 1958, Sept., v. 34, No. 3, 169–76, 4 figs. [34 refs.]

This article is a continuation of a previous one [see this *Bulletin*, 1956, v. 31, 1003]. It is highly technical and only likely to be of interest to experimental serologists; as such it does not lend itself well to abstraction. What emerges is that antigens which consist of cardiolipin, lecithin and cholesterol vary both in their sensitivity and in keeping qualities with the type of lecithin and its relative amount. For saturated (L-α-di-myristoyl) and unsaturated (L-α-di-oleyl) synthetic lecithins the latter gave higher titres than the former, but with 1·5 times less saturated than saturated it was possible to obtain the same titres, although late syphilitic sera showed less variation than sera from early cases.

With natural lecithins (beef-heart and egg) similar variations were noted but the titre responses were different; their keeping qualities also differed.

The moral to be drawn is that when a new lecithin is to be employed or when new batches are to be compared with old batches for "reference" purposes, various concentrations should be tried out and the antigens should also be tested for heat resistance.

T. E. Osmond

BOSSAK, H. N. & DUNCAN, W. P. **Method of Stabilizing Antigen Emulsion used in VDRL Syphilis Tests.** *Pub. Health Rep.* Wash. 1958, Sept., v. 73, No. 9, 836–8.

It seemed desirable for an antigen emulsion to remain stable over a period of time in order to save making a fresh emulsion each day.

To achieve this these authors added various substances to VDRL antigen emulsions and kept them at various temperatures for varying periods.

It was found that benzoic acid 0·01% in antigen emulsion (obtained by adding 0·1 ml. of 1·0% benzoic acid in absolute alcohol to 10 ml. of antigen emulsion) stabilized the emulsion for long periods.

Tests on 570 sera with fresh and stabilized antigen emulsions in parallel showed no more discrepancies than would be expected with duplicate fresh emulsions. Stabilized emulsions stored at 6–10°C. kept well for at least 6 weeks; those stored at room temperature kept

for 4 weeks and, in general, the higher the temperature the more quickly the emulsion deteriorated.

Various other substances were tried but benzoic acid proved the best. *T. E. Osmond*

SINNECKER, H. Zur Steigerung der Erfassungsbreite und Empfindlichkeit der Cardiolipinflockungsreaktion zum Schnelltest auf Syphilis. [**Increase in Sensitivity and Specificity of the Cardiolipin Rapid Test for Syphilis**] *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1958, Jan.–Feb.–Mar.–Apr., v. 4, Nos. 1/2, 54–9.

Alcoholic extracts of organs are used in the Wassermann reaction and the various flocculation reactions to give a characteristic lipoid-antilipoid reaction in syphilis. Every antibody reacts in an optimum manner only with its corresponding specific antigen and in the serology of syphilis therefore optimum results are obtained only with an antigen composed of syphilis spirochaetes. Of these, the Nelson test gives optimum results but is little used on account of expense and the laborious technique. It is therefore of great practical importance to discover which of the other serological reactions gives equivalent results. The author considers that a cardiolipin antigen is probably the most successful and describes a series of experiments in which this antigen as prepared in the Institute for Epidemiology in Berlin was compared with another similar antigen (Behring's antigen). It is claimed that the sensitivity of the Institute antigen made up with cardiolipin, cholesterin and lecithin has been increased without affecting the specificity but no details of manufacture of the antigen are given.

P. A. Clearkin

FOSTER, W. D., NICOL, C. S. & STONE, A. H. **Reiter's Protein Complement-Fixation Test. Report of a Trial in 1,000 Unselected Cases.** *Brit. J. Venereal Dis.* 1958, Sept., v. 34, No. 3, 196–7.

Tests were carried out on 1,000 unselected sera from patients attending a venereal disease department by means of the standard Wassermann reaction (WR), Price's precipitation test (PPR) and the Reiter protein complement-fixation test (RPCF); this last was similar to the WR but with a Reiter protein (commercial) antigen and overnight fixation in the ice chest plus 15 minutes at 37°C.

Results are recorded in 3 groups: (1) WR and PPR one or both positive, RPCF positive, 178; (2) WR and PPR one or both positive, RPCF negative, 13; (3) WR and PPR negative, RPCF positive, 97.

Thus group (1) showed agreement and all patients were considered syphilitic; in group (2) 8 were treated syphilitics and in 5 there was no evidence of syphilis; in group (3) 82 of the 97 patients showed evidence of syphilis, past or present, and the 15 coloured patients who gave positive RPCF reactions may well have had yaws in the past.

It is concluded that the RPCF is highly sensitive and specific, is as easy to perform as the WR and the test is suitable for routine use. *T. E. Osmond*

SCHNEEWEISS, U. Untersuchungen mit einem hitzeempfindlichen Syphilis-Orchitis-Antigen. [**Investigations with a Thermolabile Antigen derived from Syphilitic Testis (Rabbit)**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 172, Nos. 1/2, 131–4.

It is possible to demonstrate the presence of a complement-fixing antigen in the spirochaete-free supernatant from an aqueous extract of syphilitic rabbit testis. This, it is claimed, is distinct from the lipoid antigen corresponding to cardiolipin which may be extracted from syphilitic and normal rabbit testes. It is definitely thermolabile at 60°C. for 1 hour and is destroyed by acetone and ether extraction. It appears to be distinct from the antigenic elements which react with Reagin in the WR or with immobilisin in the Nelson and Mayer TPI reaction. It can be partly purified by dialysis to glycerin. *J. W. McLeod*

FIUMARA, N. J. & HILL, W. **Negative Reagin Tests in Marital Partner of Patient with Secondary Syphilis. Third Indication for** *Treponema pallidum* **Immobilization Test.** *J. Amer. Med. Ass.* 1958, Aug. 23, v. 167, No. 17, 2067–9.

It is stated that there are 3 reasons for carrying out TPI tests—(1) to distinguish between true and false positive serum reactions for syphilis, (2) to arrive at a diagnosis of syphilis in a patient who is clinically positive but serologically negative (with classical tests), and (3) in patients who give epidemiological evidence of syphilis but are clinically and serologically negative.

A case is reported of a woman who had typical secondary syphilis while her husband was clinically and serologically negative; however his TPI and TPCF tests were positive and he was treated with 6 mega units of penicillin. Thus it is claimed that the diagnosis would have been missed without these TP tests. It appears that he had probably been infected by a woman, proved to have syphilis, in July 1957, and his wife had developed secondary syphilis in October 1957.

It is of interest to note that the husband had had gonorrhoea 4 years previously [presumably treated with penicillin] and balanitis in August " of the previous summer " for which he was treated with 600,000 units of penicillin.

[If the husband had a (syphilitic) balanitis on August 5, 1957 with a positive Hinton test on August 9, treated with " 2 daily injections of penicillin ", he may easily have infected his wife; however the fact that a Hinton test on August 16 was negative is surprising and suggests that the reliability of the test was very doubtful. A good deal depends on what is meant by " the previous summer " *i.e.* previous to November 1957; does it mean the summer of 1956 or of 1957?]

T. E. Osmond

MACFARLANE, W. V. & RANNIE, I. **Gummatous Osteitis of the Skull.** *Brit. J. Venereal Dis.* 1958, Sept., v. 34, No. 3, 153–9, 12 figs.

This is a very remarkable case. Apparently the patient acquired syphilis in 1905; in 1921 ulcers appeared on the right forehead, thighs and elbows; in

1926 he reported at a venereal disease clinic with an enormous ulcer of the scalp extending from forehead to occiput. Blood reactions were positive for syphilis, cultures revealed *Proteus* and *Pseudomonas pyocyanea* and X-ray examination revealed extensive bone destruction. Treatment between 1926 and 1935 included 3 courses of arsenic and 13½ courses of bismuth which resulted in healing of the scalp. From 1949 he received 2 courses of bismuth, 12 gm. of streptomycin and 30 mega units of procaine penicillin in addition to iron, diet and vitamin therapy; the condition improved enormously for 9 months when suppuration of the scalp recurred and he died. At autopsy there was marked bone destruction, thick crusts over the ulcerated area, thickening of the dura mater, periosteal thickening of the long bones of the leg, syphilitic aortitis and amyloidosis of kidneys, spleen, liver, adrenals and bone marrow.

No real picture of this case is possible without the 12 beautifully produced figures. *T. E. Osmond*

DALLAS, N. L. **Penicillin Treatment Failures in Male Gonorrhoea.** *Brit. J. Venereal Dis.* 1958, Sept., v. 34, No. 3, 194–5.

Over a period of 7 months 447 male patients suffering from gonorrhoea (303 whites and 144 Negroes) were each treated with 300,000 units of procaine penicillin. 63 (14·1%) were treatment failures; of these 13 were classed as reinfections and 20 as relapses; the remaining 30 were probable reinfections. Qualitative sensitivity tests did not reveal complete resistance of any gonococcus strain to penicillin.

It is difficult always to distinguish between relapse and reinfection; reappearance of the gonococcus 2–3 weeks after treatment is assumed to be due to reinfection; thus the relapse rate was 4·4%.

T. E. Osmond

GARTMAN, E. **Studies in Prostatitis.** *Brit. J. Venereal Dis.* 1958, Sept., v. 34, No. 3, 181–91. [16 refs.]

The incidence, aetiology, bacteriology, treatment and prognosis of chronic prostatitis, according to this author, appear to be shrouded in mystery. It used to be thought that the condition was a common sequel to gonorrhoea, but it seems that it can appear quite independently and that often there is a large psychological component.

The author investigated a large number of (military) patients in continental U.S.A. and in Japan; he came to the conclusion that 3 methods were available—biopsy, examination of prostatic fluid and digital palpation of of the organ; he discarded the first 2 as being impracticable or useless and practised the third. Prostates were divided into 5 classes depending on the amount of encroachment into the rectum: (1) Grade 0 less than 1 cm.; (2) Grade I projecting 1–2 cm.; (3) Grade II projecting 2–3 cm.; (4) Grade III projecting 3–4 cm.; (5) Grade IV projecting more than 4 cm. [It is not stated what sort of instrument was employed to make these measurements; it does not seem likely that they could be measured with any degree of accuracy by the finger alone.]

In turn are considered asymptomatic prostatitis in healthy patients, incidence, clinical picture and treatment and acute and chronic infectious prostatitis secondary to lower urinary tract infections. In the first, occupation, sexual behaviour and monthly prevalence were all considered; in Japan regular interviews and reassurance were employed; in the U.S.A. perfunctory examination of the genitalia and prostatic palpation but not massage were employed; adjustment of psycho-sexual imbalance appeared to be the most successful treatment. In the second group treatment of the basic lesion, rather than of the prostatitis, gave the best results, antibiotics giving satisfactory responses.

A very careful study of this article is the only way of getting a real grasp of what the author means; it is evidently a very painstaking piece of work and gives much food for thought. *T. E. Osmond*

ERSKINE, D. **Lymphogranuloma Venereum. A Review of 61 Cases.** *Brit. J. Venereal Dis.* 1958, Sept., v. 34, No. 3, 163–5.

This review covers 61 cases of lymphogranuloma venereum seen at the Seamen's Hospitals, London, between 1950 and 1957. Only 4 primary lesions were seen and probably all patients except 1 were infected abroad; diagnosis depended on enlarged glands in 1 or both groins due to no obvious cause, with a positive Frei test (a dome-shaped papule, size not stated, after 48 hours) and a positive complement-fixation reaction in a dilution greater than 1 in 32; the incubation periods averaged 5 weeks. Most patients came from the West Indies, Bermuda, Cuba, South America, India and the Far East.

At first sulphapyridine for 7 days or chlortetracycline for 10 days failed to cure, but 2 courses of oxytetracycline each of 20 gm. in 10 days, with a 7-day interval, cured 19 out of 21 patients; in all, 51 of the 61 patients gave a satisfactory clinical response.

Local treatment, including surgery, is contra-indicated but aspiration was necessary in 10 patients.

Serological reactions were slow to reverse.

T. E. Osmond

MOLLARET, P. Deux maladies soeurs. La lymphoréticulose bénigne d'inoculation et la lypmhogranulomatose bénigne vénérienne (Miyagawanelloses ganglionnaires). [**Two Related Diseases: Cat-Scratch Disease and Lymphogranuloma Venereum**] *Maroc Méd.* 1958, July, v. 37, No. 398, 741–7.

In this paper the author presents his reasons for thinking that lymphogranuloma venereum (*lymphogranulomatose bénigne vénérienne*) and cat-scratch disease (*lymphoréticulose bénigne d'inoculation*) are sister diseases caused by closely-related agents belonging to the psittacosis-LGV group (*Miyagawanella lymphogranulomatosis* and *M. lymphoréticulosis*). The 2 disease processes are said to: 1. have the same clinical picture and show closely similar histological changes; 2. give specific skin tests; 3. fix complement with a psittacosis-group antigen; 4. have causative agents which are similar in size and staining properties.

[It is true that the cat-scratch skin test antigen fails to evoke a reaction in lymphogranuloma venereum and that cases of cat-scratch disease do not give a positive Frei test, but BARWELL has shown (this *Bulletin*, 1952, v. 27, 1145) that the Frei antigen is largely group in character and that the majority of cases of lymphogranuloma venereum react positively to the intradermal injection of a psittacosis-group antigen. And according to the published data available to the reviewer less than a third of cases of cat-scratch disease provide a serum fixing complement with a psittacosis-group antigen and less than half of those doing so have had titres above 1 in 20.] *S. P. Bedson*

NICOL, C. S. **Diagnosis of *Trichomonas vaginalis* Urethritis in the Male as a Routine Clinic Procedure.** *Brit. J. Venereal Dis.* 1958, Sept., v. 34, No. 3, 192–3.

Over a period of 1 year 583 male patients (466 whites and 117 Negroes) suffering from non-gonococcal urethritis were examined for the presence of *Trichomonas vaginalis*. Smears, and in 245 patients cultures, were taken from urethral discharge, urethral scrape or centrifuged urine. Positive results were obtained in 0·4% of smears, 3·7% of urines and 6·3% of scrapes and positive cultures in 8·6%. *T. vaginalis* was also found in the prostatic fluid of 3 patients who were negative to other tests; thus it was found in 5·5% of all patients. Examination of age-groups showed that those most affected were in the 30–39 and 40–49 age-groups. 18 female contacts of 17 male patients with *T. vaginalis* were examined and 15 were found infected.

As regards treatment it was found that the antibiotics used in the treatment of non-gonococcal urethritis were ineffective, but irrigations of mercury oxycyanide usually brought about cure.

In addition, of 107 male contacts of females with *T. vaginalis* 13 were found to harbour the organism.

It is concluded that cultures will disclose more cases of *T. vaginalis* in males than smears, that these tests can be carried out by clinic attendants and that infection by the organism is usually through sexual contact.

T. E. Osmond

JÍRA, J. Zur Kenntnis der männlichen Trichomoniase. [*Trichomonas vaginalis* **Infection in the Male**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 172, Nos. 3/4, 310–29, 1 fig. [Numerous refs.]

Trichomonas vaginalis infection in the female has been studied extensively but the infection in the male has not been given the same attention. Trichomoniasis though not a dangerous disease often upsets family life since it may lessen fertility and affect adversely the physical and mental health of the sufferers whether female or male. It is to be regarded as a social disease the prevention and treatment of which is as yet unsatisfactory because insufficient prominence is given to the infection in the male in the textbooks and as a study.

Trichomoniasis in the male is considered at length in this paper based on an experience of 185 cases. The technique of diagnostic examination is described at length. Specimens of secretion from the urinary meatus, the fossa navicularis, the urethra at about 2 cm. from the meatus and sometimes prostatic secretion are obtained. Microscopical examination of the unstained and stained specimens is carried out. Phase contrast microscopy is very valuable and of the staining methods the Giemsa-Romanowsky gives excellent results. The clinical picture of the infection in the male, which is of various types ranging from acute to chronic and also sub-clinical and latent, is described with references also to the literature. The parasite may become localized in the prostate, seminal vesicles, urethra and penis. Some epidemiological points which are discussed are: (1) the incubation period of the male infection ranges from 1–5 days to as long as 3–6 months but the most frequent period is 6–10 days, (2) the male is less susceptible to the infection than the female and (3) the young male is more susceptible than older men. A table sets out the frequency of trichomoniasis recorded by various authors in cases of non-specific urethritis which ranges from 1% to 73%. In the author's experience of 1,972 cases of urethritis, *Trichomonas* alone was found to be the cause in 157 of these.

The therapy of the infection is discussed. Many different medicaments have been used and the author has obtained good results with local applications of Triflocid or carbarsone. *M. E. Delafield*

OTHER COMMUNICABLE DISEASES

The order of papers in this section is as follows: Tetanus; other diseases

TOMPKINS, A. B. **Neonatal Tetanus in Nigeria.** *Brit. Med. J.* 1958, June 14, 1382–5, 1 chart. [16 refs.]

Between April 1953 and August 1956, 141 new-born babies were treated for tetanus in the Children's Department of the University College Hospital, Ibadan, and the series forms the basis of this paper.

Infants there became infected because the cord at birth is usually cut with, and dressed with, unsterile materials and because new-born babies have no immunity to tetanus even if the mother has previously had tetanus.

The incidence of the disease was found to be lower during the wet than during the dry season. On the assumption that in neonatal tetanus infection takes place very soon after birth, the age at the time of onset has been taken to represent the incubation period. Calculations on this basis revealed an incubation period averaging 7·7 days. For the 14 patients who recovered the mean was 10·7 days, and for the 121 who died it was 7·3 days. Of those with incubation periods of more than 7 days 76·4% died and of those among whom the incubation period was less than this 98·7% died, a difference which is highly significant.

The onset interval is the period which elapses between the appearance of the first symptom and the onset of the first tetanic spasm. Among those in whom a value for this could be obtained, it was found that the mean period among those who died was 0·9 days and among those who recovered 3·6 days. Mortality varied directly with severity of symptoms and it was significantly higher in the group of patients whose minimum temperature did not fall below 98°F. Sustained elevation of temperature was found to be a more serious prognostic feature than fluctuation in temperature.

The first symptom was always failure to suck from the breast and this was followed by stiffness of the body and tetanic spasms. In cases in which the diagnosis was in doubt, trismus was found to be the most reliable diagnostic sign.

The dosage of antitoxin used ranged up to 100,000 units, the whole dose being given as a single intramuscular injection. No significant difference in mortality, however, was associated with the different doses but among those receiving more than 20,000 units the survival time tended to be longer than in those receiving less than this amount. Survival time, however, was not raised by increasing the dose to 70,000 or more units and from this it can be deduced that a dose of 50,000 units of antitoxin is adequate in neonatal tetanus. The sedatives used in different cases included amylobarbitone, chloral hydrate, paraldehyde and a combination of sodium phenobarbitone with paraldehyde. The latter combination it was thought gave smoother sedation than paraldehyde alone but no convincing evidence was obtained that any of the sedatives used possessed any particular advantage over the others.

The difficulty of feeding and frequency of respiratory complications when tube feeding was employed, led to the practice of withholding food by mouth and maintaining hydration and electrolyte balance by parenteral fluid administration.

Respiratory complications accounted for some deaths and the possible value of tracheotomy in the presence of such complications is discussed. [The detailed analysis to which this—one of the largest series of cases of neonatal tetanus ever published—has been submitted, affords a valuable guide to the practical points concerned in the recognition and management of the disease. The emphasis given to its high mortality and the fact that the cause is known, should provide a fresh stimulus to health educators to increase efforts to warn parents and midwives about the practices leading to infection.] *A. W. Woodruff*

PHADKE, M. V., GODBOLE, R. E. & PANDE, S. S. **Tetanus in Pediatric Practice.** *Indian J. Child Health.* 1958, Oct., v. 7, No. 10, 675–83.

In this article the authors present an analytical study of 75 of the 108 cases of tetanus admitted to the Paediatric Unit of the Sassoon Hospital, Poona, India, during the period February 1955 to March 1958. The 108 cases represent no less than 1·8% of the total paediatric admissions.

In the group examined the case-occurrence is least in the age-group 10 days to 1 year, during which period the infant has survived the hazard of neonatal infection (mostly due to umbilical sepsis in home confinements) and enters upon a period of maximum protection from trauma, particularly that of the lower extremities, which affords the most frequent obvious method of entry for *Clostridium tetani*. In 20 cases no site of entry could be identified, and the highest proportion (28%) was associated with discharging ears, although no attempt was made to recover *Cl. tetani* from the discharge. The authors stress the point that infection is by no means confined to lesions such as deep punctured wounds; in their experience it is no less common in trivial abrasions.

The symptomatology of this group showed that trismus was present in 100%, abdominal rigidity in 65%, pyrexia in 64% and generalized convulsions in 32%. The treatment included antitoxin, after sensitivity tests, in doses of 40,000–80,000 units with penicillin and sedatives. The control of spasm has been, in the authors' experience, the most difficult problem, and they believe that, in the absence of a specialized team, the most promising results lie in the use of a sedative, such as phenobarbitone with chlorpromazine, and early resort to tracheotomy in all but the mildest cases. The mortality in this series was 33%.

[Paediatricians who are unfamiliar with the conditions of rural life in India will note with interest the authors' references to the ever-present hazard of tetanus from cow-dung (which is commonly used to give a smooth finish to the mud floor of a peasant's living quarters) and from the custom of children going bare-footed in and out of doors.] *E. S. Phipson*

VAN ROOTSELAAR, F. J. Naveltetanus behandeld met chloorpromazine. [**Umbilical Tetanus treated with Chlorpromazine**] *Nederl. Tijdschr. v. Geneesk.* 1958, Oct. 25, v. 102, No. 43, 2097–8.

The English summary appended to the paper is as follows:—

"At the age of 11 days a baby suffering from umbilical tetanus was treated with chlorpromazine, which completely suppressed the convulsions. On discontinuation of chlorpromazine the convulsions returned; reinstitution of chlorpromazine therapy caused immediate improvement. After 16 days the child was free of symptoms without chlorpromazine; it was discharged as cured after 19 days."

MILLER, C. L. & STOELTING, V. K. **Recent Evaluation of the Treatment of Tetanus.** *J. Amer. Med. Ass.* 1958, Sept. 27, v. 168, No. 4, 393–4.

Before 1955 curare had been used at the Indiana University Medical Centre for the treatment of tetanus. Since 1955 curare has not been used; instead, barbiturates and promezathine have been used with success. Secobarbitone (Seconal) and pentobarbitone (Nembutal) have been the drugs used and have been given intramuscularly. The addition of promezathine has decreased anxiety in the patient. When tetanus is suspected, an anaesthetist is asked to begin sedation and a prophylactic tracheotomy is performed. The

object of treatment is clearly stated as the prevention of asphyxia by controlling spasm and the provision of good supportive treatment. [The abstracter agrees entirely that curare is not the drug of choice in tetanus and that most cases, even if severe, can be controlled with sedation. There seems no valid reason for giving the barbiturates by repeated intramuscular injection as it is usually possible to leave a gastric catheter in position in most cases of tetanus. Prophylactic tracheotomy seems a rather extreme measure.]

A. B. Christie

SCHAUB, F. & ZIMMERMANN, E. Coronare Durchblutungsstörung nach Tetanusantitoxin-Injektion. **[Allergic Coronary Damage after Injection of Tetanus Antitoxin]** *Ztschr. f. Unfallmed. u. Berufskrankh.* 1958, Sept., v. 51, No. 3, 238–41, 1 fig. [18 refs.]

The patient was a man of 43 with hypertonia and latent diabetes.

ZOONOSES

In this section the abstracts are arranged as far as possible in the following order: General; Anthrax; Brucellosis; Tularaemia; Leptospirosis; Ornithosis; Others.

For such tropical diseases as Trypanosomiasis, Leishmaniasis, Rickettsial Fevers, Yellow Fever, Plague, etc., see TROPICAL DISEASES BULLETIN.

CARITHERS, H. A. **Pets in the Home: Incidence and Significance.** *Pediatrics.* Springfield, Ill. 1958, May, v. 21, No. 5, 840–48. [45 refs.]

The pet population in the United States of America is large—about 24 million dogs, 28 million cats and 15 million birds. In the author's practice, 300 parents were questioned about their children's pets; 95% were found to be intimately exposed to dogs, and 90% to cats. It is suggested that adult animals would prove safer pets than young ones because immunity has arisen in the former. The subject of the zoonoses is then discussed in relation to North American children, and the following are regarded as of some importance—*viruses*: cat scratch disease, rabies, psittacosis, arthropod-borne viruses, and encephalomyocarditis; *bacteria*: salmonellosis and leptospirosis: *fungi*: skin forms only such as *Microsporum canis, Tinea corporis; parasites*: visceral and cutaneous *Larva migrans.*

P. C. C. Garnham

ALIVISATOS, G. P., DERDEMESIS, V. & EDIPIDES, T. Epidemiologische Studien über Brucellosis mit Hilfe eines *Brucella*-Coombs-Testes. **[Epidemiological Studies on Brucellosis with the Help of *Brucella*-Coombs-Test]** *Ztschr. f. Immunitatsf. u. Exper. Therap.* 1958, July–Aug., v. 116, Nos. 1/2, 173–201. [16 refs.]

During an investigation into an epidemic of undulant fever in an endemic area (Epirus) which began in 1950–1 and still continues, the greater number of the people then examined were re-examined in 1956–7 and the results up to date are reported in this paper.

In a region free from the disease introduction of fresh animal infection was followed by an acute epidemic in which persons of all ages, though less frequently children of 0–4 years, were attacked. After a period of time, usually 3–5 months, the epidemic ceased, and although the epizootic continued its character changed and it became enzootic with occasional epizootic outbreaks.

Sera were first tested against suspensions of *Brucella melitensis, Br. suis* and *Br. abortus* in 0·9% saline (Antigen A) and in 10·0% saline (Antigen B). The serum dilutions were made with 0·5% saline. No difference was observed in the results of agglutinations given by the suspensions made from all 3 organisms, and in consequence the tests were performed with a single suspension made from *Br. bovis* 99. The *Brucella*-Coombs-Test was performed in the usual manner with rabbit anti-human-globulin serum. The melitin test was performed with a filtrate from a 28-day broth culture of *Br. melitensis* diluted with an equal quantity of normal saline.

The second series of observations were carried out 5½–6 years after the first; in the latter 1,088 persons were examined and in the former 964. Many details and tables are given of the results of these investigations, which are summarized as follows.

In such an endemic region *Brucella* infection developed in a different manner from that in surroundings where the infection appeared suddenly for the first time. In the latter instance acute cases were almost always among old people. The sudden outbreak decreased, however, after a few months and its place was taken by an endemic animal infection. As a result of the persistent opportunities for infection some of the people contracted a sub-clinical chronic infection as shown by the melitin reaction and repeated agglutination tests. Children in the age-group 0–14 years, although infected as shown by the agglutinin and melitin reactions, were very seldom ill. The older age-groups were protected by a raised resistance or immunity due to a "dumb" infection. Thus there are persons in the age-group 15–49 who do not become ill in spite of chronic infection but who, after the age of 50 and over, develop the illness. It is apparent that not all people are susceptible when exposed to infection and this can be due to an allergic condition. This raised resistance can be broken by superinfection or by auto-infection, leading to illness. The superinfection comes directly from livestock. There is therefore no true immunity to brucellosis, but there is an allergic condition as in tuberculosis. This allergic condition apparently can disappear; it is certain that the agglutinins can disappear. Moreover, in the serum of persons who are infected but suffer no illness, incomplete antigens only are present. It is possible that complete antibodies and normal agglutinins had been present but had disappeared. A retrospective diagnosis in a given case may be made by the disappearance of normal agglutinins and the presence of incomplete antibodies.

Agglutinins, both normal and incomplete antibodies,

disappeared more rapidly from patients treated with antibiotics than in those treated with *Brucella* vaccine or under palliative treatment.

It is essential to carry out the *Brucella*-Coombs-Test along with the normal agglutination reaction in any investigation of brucellosis, as this provides a better diagnosis and contributes to the solution of questions on the allergic state and raised resistance.

P. A. Clearkin

PEERY, T. M. & EVANS, J. M. **Brucellosis and Heart Disease. III. Chronic Valvular Heart Disease following Nonfatal Brucellosis.** *Ann. Intern. Med.* 1958, Sept., v. 49, No. 3, 568–79. [23 refs.]

In a previous communication [this *Bulletin*, 1958, v. 33, 746] the senior author reviewed the incidence of aortic calcification in fatal brucellosis. Endocarditis was found to be the commonest cause of death in brucellosis. The present article concerns patients in whom brucellosis did not cause death but in whom cardiac lesions followed brucellosis. The author reviews the literature on the association of cardiac disease and brucellosis and gives the clinical histories of 10 more patients showing this association. In 4 the recognition of valvular disease followed illnesses diagnosed as brucellosis; "the remaining cases come to light by searching out patients with a history of brucellosis and studying them for evidence of residual cardiac disease". The aortic valve was affected in 9. From none of the patients were *Brucella* cultured and the evidence from serological and skin sensitivity tests in some cases was slender. The authors consider that brucellar endocarditis is particularly liable to occur in those with a history of long occupational exposure to brucellosis and that it is prone to lead to calcific aortic stenosis.

[This association between brucellosis and aortic valvular disease calls for further observations but in the absence of statistics as to the number of cases reviewed it is difficult to exclude aortic valvular disease of other origin having been found in patients giving a history of previous brucellosis.] *Frederick J. Wright*

Diseases due to Fungi

For papers on systematic mycology, see the section in Bacteriology, below. Papers on Blastomycosis (South American type), Coccidioidomycosis, Mycetoma and Rhinosporidiosis are abstracted in the TROPICAL DISEASES BULLETIN

BENEDEK, T. **Selective, Chemical Epilation in the Treatment of Tinea capitis as contrasted with the Diffuse X-ray Epilation.** *Mycopathologia.* The Hague. 1958, June 2, v. 9, No. 2, 97–110, 1 fig.

X-ray epilation remains the most efficient method of treatment for ringworm of the scalp caused by *Microsporum audouini*. For mass treatment, however, the absence of a sufficient number of X-ray sets and the lack of trained personnel makes this method unsuitable. Many parents, moreover, object to the irradiation of their children's heads and subsequent baldness. The public have become increasingly aware of the risks of radiation therapy.

In the search for other remedies, a number of different antifungal compounds have been tried. Unfortunately, fungicidal and fungistatic properties demonstrated by *in vitro* experiment could in no case be duplicated in clinical practice.

A remedy to be used for treatment of the scalp at home must fulfil 2 requirements; (1) the method has to be as simple as an ordinary hair wash, (2) it has to work with sufficient rapidity in order to eradicate the infection before the mothers of these children become tired of the procedure and before further contact infection could be caused. Inability to penetrate the hair follicles was responsible for the failure of all these compounds. It was therefore necessary to try and imitate X-ray epilation rather than to attempt to kill fungi which were out of reach in the recesses of the follicle.

A method was sought which was, (1) absolutely selective, attacking only the affected hairs, (2) clean and did not prevent the use of Wood light, (3) simple in application, (4) curative in the shortest possible time and (5) harmless causing no local irritation or systemic involvement.

The following compound, tested over a period of 8 years, completely filled the above requirements:—

Copper sulphate	5%
Chloral hydrate	5%
Glycerin	78%
Sodium lauryl sulphate	1%
Aq. dest.	11%

In vitro tests showed that this compound had some fungicidal and some fungistatic properties, and its efficiency was fully demonstrated by clinical trials. The first communication was based on its use in 96 cases, 90 being due to *M. audouini* and 6 to *M. lanosum*. Since then it has been used on 153 other cases. It proved most effective in the epidemic of ringworm at Sault St. Marie, Ontario. Of 849 cases 551 were negative within 6 weeks. After 2 to 4 weeks' conscientious treatment all the infected hairs become

loosened simultaneously and either fall or can be easily brushed out.

This compound showed no irritant or sensitizing properties and did not affect normal hair. Simple instructions are included by the author for the use of those carrying out home treatment:—

"A. Boys

"1. Clip the hairs on the entire scalp before treatment begins and every week thereafter. Hand clippers or scissors should be properly cleaned, and, sterilized after use. Clipped hairs should be carefully collected and burned to prevent further spread of infection.

"2. Apply the solution to the infected area(s) or to the whole scalp as the case may be. A few drops of the Compound are poured on the infected area(s) repeatedly and rubbed in with a soft tooth brush for 2 to 3 minutes, twice daily, morning and evenings.

"3. Boys must constantly wear a stocking cap, day and night: (a) to keep the solution on the scalp; (b) to prevent the spread of infection. Scullcaps should be changed at each shampooing. The used ones should be boiled for 10 minutes and washed, then, they are suitable for use again.

"4. After every third rub the whole scalp will be shampooed with either a shampoo or any good soap and the infected areas rubbed off for 2 to 3 minutes with a soft hand brush, 3″ × 1″ in size, to better enable removal of loose hairs.

"5. Following the shampooing, the scalp should be dried completely and the Compound rubbed in again.

"6. This simple cycle should be repeated until the doctor advises that the treatment be discontinued.

"7. Only the doctor can tell that the ringworm disease is cured.

"B. Girls

"The procedure, with one exception, is exactly the same as for boys. However, in the case of girls, total clipping of the scalp can be dispensed with. It is, however, reasonable and expedites the whole treatment, if and when single larger patches are clipped every week and, of course, before the treatment begins. The rest of the hair covers up these clipped areas. If the infected areas are larger or they are exposed at the temples, for instance, the girls should also wear stocking caps.

"Both boys and girls should never use each others' comb or brush and the infected child should sleep separately in his or her own bed, if possible.

"These simple instructions are handed out to the parents in each case. Besides, the whole procedure is thoroughly explained by the doctor and, in every instance, the method is demonstrated as to how the Compound shall be applied and rubbed in."

H. T. H. Wilson

FOWLER, W. *Candida albicans* **Urethritis. Report of a Case.** *Brit. J. Venereal Dis.* 1958, Sept., v. 34, No. 3, 166–8, 1 fig.

The patient was a married man of 54 years who denied extra-marital intercourse; he complained of urethral discharge and irritation and slight frequency.

On examination there was a scanty thin mucopurulent discharge and the urine showed: glass I haze and many thick white heavy threads; glass II clear, few threads; glass III clear. Urethroscopic examination showed large white excrescences on the mucosa (well shown in a drawing); microscopically mycelia and spores of *C. albicans* were seen and a profuse growth occurred on Sabouraud's medium; the urine contained 2% glucose and the blood-sugar was 350 mgm.%.

Treatment consisted of the instillation of 3 ml. of diamidophenylamine dihydrochloride (M & B 938) each day for 3 days, and there was considerable improvement before diabetic treatment was started. The condition cleared completely in less than 3 months. How far cure was due to local treatment and how far due to diabetic treatment is not clear; it does seem that modern fungicides may prove effective in this vary rare condition. *T. E. Osmond*

REID, J. D., CABLE, J. V. & LAURENSON, G. R. **Histoplasmosis. A Report of Cases in New Zealand.** *New Zealand Med. J.* 1958, Aug., v. 57, No. 320, 325–7, 5 figs. on 2 pls. [14 refs.]

"Each of the three patients had lived extensively outside New Zealand and in none can the disease, if accepted as histoplasmosis, be ascribed to infection within this country. Nevertheless, it is likely that the disease is present and will be found. A small series of some six cases of atypical pulmonary calcification has been skin-tested to histoplasmin at the Mass Miniature Radiography Unit in Wellington; none has been positive. (Personal communication Dr. M. C. Laing.) A similar number has been tested at this hospital with only two positives as reported above. Review of histological preparations of six patients with caseating adrenal glands and Addison's disease has not shown another example of histoplasmosis, nor has it been found on special staining of seven caseous pulmonary lesions selected for review because of their largely solitary character; all of these had acid fast bacilli in sputum and gastric juice or in the resected granuloma."

Summary

"A case of histoplasmosis of the adrenals is reported with mention of two probable cases diagnosed by chest *x*-ray and positive histoplasmin skin test. The main features of the disease are briefly reviewed."

Rheumatic Diseases

HALLIDIE-SMITH, K. A. & BYWATERS, E. G. L. **The Differential Diagnosis of Rheumatic Fever.** *Arch. Dis. in Childhood.* 1958, Aug., v. 33, No. 170, 350–57. [24 refs.]

The differential diagnosis of rheumatic fever may be very difficult in some of its milder forms. Yet in view of the continuous daily sulphonamide or penicillin prophylaxis now recommended nationally and internationally for the prevention of further attacks of rheumatic fever, it has become increasingly important to recognize mild cases of rheumatic fever.

The differential diagnosis is discussed from the experience gained in the unit at Taplow over the period 1947–56. The original diagnosis is reviewed in a 1 in 6 sample of the cases ultimately diagnosed as rheumatic fever, and 12 are described which were originally diagnosed otherwise. The original diagnoses were: poliomyelitis, pneumonia, meningitis, rubella, dysentery, subacute bacterial endocarditis, appendicitis, suppurative arthritis of hip, Still's disease and fallen arches. In all these cases the subsequent development of arthritis or other clear sign of rheumatic fever established the diagnosis.

A larger series of 196 patients is described who were originally thought to have rheumatic fever, but in whom the diagnosis was eventually not substantiated. This series is classified in 7 main diagnostic groups: functional, traumatic and postural, infectious, connective tissue disorder, rheumatic and congenital heart disease, blood dyscrasia, and others. The common erroneous interpretations of history, fever, tachycardia, and systolic murmurs are discussed. It is concluded that a more critical examination of the patient, increased awareness of the significance of the physical signs elicited and fuller investigations, notably of sedimentation rate and of evidence of streptococcal infection, would be helpful in the less obvious cases.

H. Stanley Banks

KAPLAN, S. **Oral Phenoxymethyl Penicillin Therapy in Prophylaxis of Recurrent Rheumatic Fever.** *J. Dis. Children.* Chicago. 1958, Sept., v. 96, No. 3, 288–93. [20 refs.]

Phenoxymethyl penicillin (penicillin V) was given orally in doses of 125 mgm. daily for 2 years to 266 children who had had at least one episode of acute rheumatic fever. There were no toxic reactions and the incidence of rheumatic recurrence or beta haemolytic streptococcal infection was low. *A. B. Christie*

See also p. 151, HSU & EVANS, **Untoward Reactions to Benzathine Penicillin G in a study of Rheumatic-Fever Prophylaxis in Adults.**

Heart Disease

PUFFER, Ruth R. & VERHOESTRAETE, L. J. **Mortality from Cardiovascular Diseases in Various Countries, with special reference to Atherosclerotic Heart Disease. A Preliminary Analysis.** *Bull. World Health Organization.* Geneva. 1958, v. 19, No. 2, 315–24, 3 figs.

Age-sex specific death rates for various countries in 1954, ranging from Finland to Guatemala, have been collected and compared. More specifically, rates are given for four groups taken from the International Classification of Diseases, Injuries, and Causes of Death:—

(1) Arteriosclerotic degenerative heart disease.
(2) Vascular lesions affecting the central nervous system.
(3) Other diseases of the heart.
(4) Certain other diseases of the circulatory system.

The rates, particularly for arteriosclerotic heart disease, vary widely with high rates in Finland, U.S. and countries in the British Commonwealth such as New Zealand, and lower rates in France. In the countries with high rates, the proportions of deaths from each group are much the same. In Japan, on the other hand, over two-thirds of the cardiovascular deaths were due to vascular lesions of the central nervous system; and in the Latin American countries these proportions vary considerably. The authors speculate on the possible reasons for these very material discrepancies. Some of the differences may derive from the differing geographical spheres of influence of the various schools of clinical medicine and their methods of classifying cardiovascular disorders. A comparison of the age specific trends in the two sexes for U.S.A., France and Mexico, however, shows that the sex ratio is not the same at different ages and varies between countries in a way which is unlikely to be entirely due to divergent diagnostic and classificatory practice. The interpretation of such data is both difficult and important and the authors emphasize the need for further study of the conformity or lack of it in the classification of cardiovascular diseases. *D. D. Reid*

Occupational Hygiene

In this section the abstracts are arranged as far as possible in the following order : General; Mining and Dust Diseases; Poisoning due to Metals, Solvents and Other Substances; Skin and Other Affections; Radio-active Substances; Other Conditions; Occupational Psychology

MINISTRY OF LABOUR AND NATIONAL SERVICE. **Annual Report of the Chief Inspector of Factories for the Year 1957** [MCCULLOUGH, T. W.]. Cmnd. 521. 91 pp. 1958. London: H.M. Stationery Office. [5s.]

This report is shorter than in previous years, and in comparison with earlier reports its scope is restricted. The objects of shortening the report have been to reduce the burden of preparation, to simplify the report, and finally to reduce its cost and ensure earlier publication. A separate report on industrial health is to be published.

In 1957 the numbers of reported accidents and of fatal accidents both fell by over 5%. Particular attention has recently been paid to accidents in the building industry, and it is satisfactory to find a decline of 16% in the number of fatal accidents in that industry. Despite the specific prohibition by the Factories Act of the cleaning of machinery in motion, 428 women and young persons were injured through such activity in 1957.

Grease solvents in general use are either inflammable and non-toxic, or toxic and non-inflammable. Fluorinated hydrocarbons which are now being made on a small scale have good solvent properties, and some of them are both non-toxic and non-inflammable. It is hoped that with increasing demand they will become less expensive, and then displace some of the hazardous substances now widely used. Several examples are given of the replacement in industrial operations of dangerous materials by others less dangerous.

Much attention is being given to the control of dust in foundries. Dust from pedestal and swing-frame grinders has been satisfactorily controlled, new systems have been introduced for the control of dust at mechanized knock-out points, and the low-volume, high-velocity method of local exhaust ventilation has been applied to a large range of portable tools.

There have been important developments in the use of special steels for lifting appliances.

For more than half a century the Factory Inspectorate has cooperated with various outside bodies and individual workers in research work concerned with industrial health and safety. This report contains a chapter which outlines some of the work recently done in this way. A further chapter deals with safety training in industry.

The report ends with a series of 14 statistical appendices *Thomas Bedford*

SWANN, P. G. **Some Results from the Periodical Medical Examination of Executives in Industry.** *Trans. Ass. Indust. Med. Officers.* 1958, July, v. 8, No. 2, 61–2. Discussion 63.

The author asserts that the foundation of personal preventive medicine is the periodical medical examination to diagnose unsuspected disease and correct errors of living and working. Examinations can fall into disrepute if conducted in a too hurried or routine manner. The emphasis should be on health and the examination can do much to reassure the executive.

Details are given of the nature of the examination (1 hour's duration) and results found in a non-selected group of 200 (all volunteers). 65% were entirely normal [no definition of normal is given], 11·5% had a sustained blood pressure of more than 160/90 without symptoms, 2% had symptoms associated with hypertension, 9·5% were 10–20 pounds overweight, according to Metropolitan Life Assurance tables.

In the discussion it was admitted that 15% had some disease for which a doctor had already been consulted, but the author did not think examination by the company doctor raised any problem of medical ethics.

T. O. Garland

NORMAN, L. G. **The Health of Bus Drivers. A Study in London Transport.** *Lancet.* 1958, Oct. 18, 807–12, 8 figs.

Dr. Norman is exceptionally well placed to speak with authority on the health of a working group, for by 1958 there were 87,000 on the payroll of London Transport of whom 20,250 were drivers. The minimum age of these men is 24, a few work over the age of 65, all retire by 70.

Drivers are examined before acceptance, after any absence beyond 28 days, after any absence due to accident, after any significant occurrence such as fainting, and annually after the age of 65. In addition there are eyesight tests at ages 50, 55, 58, 60, 62, 64 and thereafter annually.

Selection and training are considered the most important measures for preventing accidents; only 50% pass the selection interview. Details are given of the medical examinations with eyesight tests. About 20% fail these, half of the failures being due to visual defects.

Training concentrates on relaxation and anticipation rather than quick reaction and 20% fail to complete the course, so that finally only 1 in 4 applicants obtains a licence.

Both drivers and conductors suffer more short-term sickness (absent from work less than 4 days) in the younger age-groups, though this phenomenon is much more marked in the conductors. In the over 40 age-group, however, there is a sharp rise in sickness absence of over 4 days duration; *i.e.* the older man stays away less often but for a much longer time, so that by the age of 60 total sickness absence is 4 times that at 30

for both conductors and drivers (5·2 days per year at age 25–29, 20·1 days per year at age 60–64 for drivers, rather more for conductors).

Bronchitis causes 3·7% of the sickness absence in drivers at age 30–34, and no less than 17·3% at 60–64. Absence due to disease of stomach and duodenum is higher in drivers and conductors than in workshop staff except at ages 40–44. Possibly the most significant variable is a much greater amount of shift work for those on the buses.

There is a steep rise in functional nervous disorders among conductors around the age of 50. By the age of 60 this disparity with drivers and workshop staff has disappeared—possibly the nervy conductor gives up before then.

Norman concludes this valuable study with a review of loss of consciousness in drivers—the one incident all hope to avoid. In 20,000 drivers over a working period of 11 years, 28 cases have occurred, 10 due to coronary thrombosis, 18 due to other causes. In 15 cases among the latter group, the bus was still moving, yet there was loss of life in only 2 instances. In 5 of the coronary cases the driver died suddenly without stopping, resulting in 3 accidents.

T. O. Garland

GLORIG, A., Jr. & SUMMERFIELD, Anne. **Noise—is it a Health Problem?** *J. Amer. Med. Ass.* 1958, Sept. 27, v. 168, No. 4, 370–76, 2 figs.

"Today misconceptions about the hazardous effects of noise are rife. It is the purpose of this paper to expose some of these misconceptions and to outline the factual information that is available to help us realistically assess the effects of noise exposure." To this end the definition of "noise" is discussed. "Definitions of noise based on the physical characteristics of sound have not been satisfactory because the definitive characteristic of noise is not physical but psychological, namely its undesirability." The currently accepted definition is "Noise is any unwanted sound". The measurement of sound is described in general terms and it is pointed out that although measurements of sound pressure may be used to indicate the amount of noise it is important to "remember that the amount is not the same as the energy of the noise".

The known effects of noise exposure are of 2 types—non-auditory and auditory. The non-auditory effects are discussed under the headings of: (1) speech interference, (2) annoyance, (3) possible loss of efficiency and (4) physiological changes which occur as emergency reactions in response to sudden sharp sounds. The auditory effects—temporary and permanent—are considered at some length. It is concluded that the non-auditory effects produced by typical noise exposures "do not constitute a health hazard. Whether the non-auditory effects of the extremely high noise levels generated by jet engines and rocket engines will constitute such a hazard remains to be seen". The auditory effects of noise exposure, however, are a serious threat to health of a large segment of the industrial population. Much is known about the relations of hearing loss to different levels and periods of noise exposure and by this knowledge "noise-induced hearing loss can be either prevented or greatly minimized". The organization of programmes of hearing conservation is described in some detail but with emphasis on the need for further scientific study of the problem of noise.

M. E. Delafield

LANDWEHR, M. & WIEGAND, H. Die Silikosegefährdung von Röstern im Siegerländer Eisenerzbergbau. Medizinische und mineralogisch-staubtechnische Untersuchungen. Zur Frage der Staubschädigungsmöglichkeit durch die Einwirkung oxydischer Eisenerzstäube auf die menschliche Lunge. [**The Exposure of Roasters to Silicosis in the Siegerland Iron ore Mines. Medical Investigations and Mineralogical Examination of the Dust. The Effect of Iron Oxide Dust on the Pneumoconiosis Risk**] *Beiträge z. Silikose-Forschung.* 1958, No. 55, 1–47, 20 figs. [18 refs.]

Workers handling iron ore at a plant where it was calcined and subjected to magnetic separation were exposed, in some cases, to dust containing appreciable quantities of quartz. The silicotic changes revealed by X-ray examination were, however, only slight although exposures of many years' duration were recorded.

A number of dust samples was examined microscopically and the proportion of quartz particles determined on a surface area basis.

In the pure ore the quartz content was low and occurred mainly in coarse particles. Poorer ores contained more quartz and rock particles which were found in all sizes. After calcination a strong tendency of the dust to coagulate was observed and the air-borne concentrations were always low. It is concluded that the iron oxide reduces the potency of the quartz by a factor of 0·01.

C. N. Davies

SCHWARZ, W. & MERKER, H. J. Elektronenmikroskopische Untersuchungen am Bindegewebe der Lunge, des Mesenterium und des Omentum der Ratte. [**Electron Microscope Observations of the Connective Tissues of Lung, Mesentery and Omentum of Rats**] *Beiträge z. Silikose-Forschung.* 1958, No. 54, 1–14, 4 figs. [16 refs.]

In experimental silicosis discrepancies are sometimes observed when different types of connective tissue are used to measure the fibrogenic properties of dusts. The senior author had previously studied the development of normal reticulin and collagen in tissues by electron microscopy [this *Bulletin*, 1957, v. 32, 457], and he thought that the type of fibril present in different kinds of connective tissue might be related to the differences in reaction.

The present paper gives a detailed description of the fibrous tissue found in lungs, omentum and mesentery of rats aged 10 weeks.

The chief criteria used were the amount of cementing material in relation to fibrils, the periodicity of the fibrils, their thickness and their behaviour towards silver staining. The technique used was to cut sections, after formalin fixation, of about 2 micron thickness, to disintegrate them by ultrasonic treatment, to wash the material and to repeat the ultrasonic and washing treatments several times.

It was found that all 3 materials gave similar fibrils which corresponded in their development to reticulin, *i.e.* periodicity of 500–560 Å was usually visible, there was some cement left after washing, the fibrils were of the order of 20–50 millimicrons in thickness, and silver was adsorbed externally in regular periodicity.

The chief criterion used to differentiate the fibres from lungs, omentum and mesentery was the distribution of thickness of fibrils, and this is shown in the form of block diagrams in the paper. Omentum was more similar to lung than to mesentery, and the same held for the degree of periodicity of silver adsorption which was best developed in lung fibrils and least in those of the mesentery. The observations are illustrated by a number of electron micrographs.

It is concluded that the omentum would be the most suitable locality in the peritoneum for getting reactions similar to those seen in the lungs, and that the type of (precollagen) fibril present in connective tissue must be considered when evaluating the results of tests in experimental silicosis. *G. Nagelschmidt*

MOSINGER, M. Une conception pathogénique de la silicose. Le rôle du système neuro-ergonal. [**A Concept of the Pathogenesis of Silicosis. The Rôle of the Neuro-Ergonal System**] *Arch. Malad. Professionnelles.* Paris. 1958, July–August., v. 19, No. 4, 356–72.

Fundamental research into silicosis should basically be directed towards the prevention and treatment of the disease. Prevention involves control of the dust and increase of the resistance of the workman to the noxious agent. Treatment comprises the elimination of the dust and the inhibition of fibrogenesis. In the production of silicosis there have been 3 main hypotheses; mechanical, chemical and immunological, none of which is wholly acceptable. Commencing in 1930 Mosinger and his co-workers in France have concentrated on the constitutional reaction of the organism to the aggressive agent. The mechanism, to which they have given the name neuro-ergonal, is highly complex. It comprises the intricate combined action of the nervous and endocrine systems. The many aspects of the problem are so diverse and involve so many scientific disciplines, that they are beyond the skill of any single research worker. The need is for research teams in the fields of chemistry, biochemistry, physiology, human and experimental pathology, neuro-endocrinology, endocrinology, enzymology, vitaminology and clinical medicine. The supreme need is that the work of these separate disciplines should be coordinated and integrated under the direction of a central organization, which must have ample resources.

[Clinicians have long observed that certain workmen develop silicosis more rapidly or more seriously than their fellows, apparently similarly exposed to the risk. These patients are regarded as unduly susceptible. This fact does not signify that these individuals are constitutionally vulnerable. Some persons, owing to anatomical defects of the upper respiratory apparatus, are mouth-breathers. In others the lungs are already damaged by antecedent disease, which despite thorough clinical pre-employment examination, cannot always be detected. Also, while we can measure environmental conditions generally, we are unable to assess precisely the risks to which individual workmen have been exposed. We do not know the effect of short intensive episodes of dust inhalation in the course of years of employment at risk.] *A. Meiklejohn*

KAMOHARA, Y. **The Production of Antibody by Quartz administered parenterally.** *Kyushu J. Med. Sci.* 1958, Feb., v. 9, No. 1, 46–60, 1 fig. [20 refs.]

In the introduction to this paper the author reviews some of the current literature on the question of antibody formation in silicosis and antibody-antigen reactions as the pathogenesis of the disease. He particularly quotes the hypothesis of JAEGER and SEIFERT that protein adsorbed on the crystalline lattice of quartz is transformed to fibres; and the work of SCHEEL who showed that quartz particles adsorb and denature egg albumin and that intravenous injection of the coated particles gives rise to anti-egg-albumin antibodies. The author feels that Scheel's work substantiates the Jaeger-Seifert hypothesis and hopes that by extending the work of the former he may further substantiate the theory of the latter.

The experiments were conducted largely after the methods of Scheel. Quartz particles were coated with rabbit serum *in vitro* and repeatedly injected intravenously into rabbits. The sera of the rabbits were tested for the presence of antibodies by looking for agglutination of rabbit serum-coated-quartz particles by the serially diluted sera. Antibodies appeared about 2 months after the first injection, reached a maximum titre of 1/128 at 5–7 months, and slowly declined thereafter. Repeated intravenous injections of uncoated quartz particles similarly gave rise to antibodies in rabbits. Intrapulmonary injection *via* the trachea also gave rise to antibodies in rabbits that were of a titre of 1/64 to 1/32, appearing 1 year after the injection and persisting for 1½ to 2 years.

The antibodies that appeared in response to intravenous uncoated quartz particles could be cross-agglutinated with, and adsorbed by, the proteins adhering to quartz particles after they had been exposed to human, horse and bovine sera. The antibodies were also shown to be heat resistant (58°C. for 1 hour) and active only between *p*H 5·0 and 8·5.

Experiments were conducted in which rabbit serum was treated with aerosil solutions and then used as antigen in a precipitation tests with sera known to contain quartz-induced antibody. No reaction was demonstrated.

Attempts were made by the same methods to show a difference between rock crystal and quartz by demonstrating a difference in the specificity of the antibodies produced in response to each. [The author's claims to have demonstrated this are not altogether convincing.

Most of the experiments described are confirmatory of work published by other authors. The theoretical considerations and interpretation of results are plausible but are difficult to follow, partly owing to the author's English usage, and are often circumlocutory.]

P. D. Byers

CLERICI, E. & BAIRATI, A. Azione del quarzo sulla ricostituzione di fibrille collagene dalle soluzioni. [**Action of Quartz on the Reconstitution of Collagen Fibrils from Solutions**] *Med. d. Lavoro.* 1958, Aug.–Sept., v. 49, Nos. 8/9, 485–93, 2 figs. English summary (8 lines).

The authors point out that in 1942 VON BUZAGH noted that quartz was capable of adsorbing an unidentified fraction from collagen solutions, leaving a residuum which could not be precipitated by salts, but that if part of the quartz on which the fraction was adsorbed was again added to the solution, after the addition of Na acetate collagen fibre formation started once again.

As this might have implications in the genesis of silicotic nodules, the authors have taken up von Buzagh's work and in this report deal with fibrillogenesis from acid solutions of collagen (rat's tail tendon) before and after quartz adsorption [for the considerable technical procedures see original paper].

The results showed that: (1) solutions of natural collagen are not pure, as in the majority of cases it does not form more than 85% of the total protein present; (2) in solutions of rat's tail tendon the treatment of collagen solutions by quartz induces a massive diminution of the proteins in solution; (3) redissolving the material adsorbed on the quartz in acetic acid and adding Na acetate to the solution does not cause fibrillogenesis. Hence the substance in contact with the quartz undergoes such changes as to prevent new fibre formation.

The authors conclude that the lack of reconstitution of fibres from such solutions is due to the capacity of quartz to adsorb collagen, thus reducing the concentration to so low a level that it is not acted upon by precipitating agents. *W. K. Dunscombe*

HASSELT: INSTITUT D'HYGIÈNE DES MINES. Communication No. 155. Action des poussières et d'agents pharmacodynamiques sur la fonction respiratoire. 6e partie. Resultats des aérosols d'acétylcholine dans un groupe de 182 houilleurs [**The Action of Dusts and Drugs on Respiratory Function. Part 6. The results of a Study of Acetylcholine Aerosols in a Group of 182 Coal-Miners**] [MINETTE, A. & VAN WYMEERSCH, L.]. 1958, Aug. 15, v. 13, No. 6, 30 mimeographed pp., 7 figs. [11 refs.]

At the Institut d'Hygiene des Mines at Hasselt, Belgium, research workers are pursuing a programme of investigation into the action of dusts and various drugs on respiratory function. The present study—the 6th in the series—concerns the reactions observed following the inhalation of acetylcholine aerosols. Observations were made on a group of 182 coal-miners, but in the course of the experiment 36 were rejected, leaving 146. Of these, 27 had no radiographic evidence of pneumoconiosis; the balance comprised 96 with simple and 23 with complicated pneumoconiosis. Care was taken to ensure that none had ever suffered any allergic disorder. The controls consisted of 35 normal workmen, likewise free from allergic disturbance, and 36 men with chronic bronchitis and asthma of non-occupational origin. At the outset all were examined clinically, with particular reference to cough and adventitious sounds in the lungs. Pulmonary ventilation was recorded by Tiffeneau's method. Under very precisely standardized conditions each subject inhaled an aerosol solution of acetylcholine (0·5%) for 30 seconds. Thereafter the patients were re-examined. It was not possible to measure precisely the severity and duration of cough and the presence of adventitious pulmonary sounds. They were recorded broadly (+; ++; +++). As to pulmonary ventilation, a positive reaction was not admitted unless the diminution amounted to at least 10% of original measurement.

Of the 146 subjects, 53 had a positive ventilation reaction and 62 a positive cough response, but in only 31 were these reactions combined. The reactions noted in the miners were similar to those in subjects with chronic bronchitis but much less than those observed in the men with asthma. *A. Meiklejohn*

SCHEPERS, G. W. H. **The Influence of Fiberglas-Plastic Dust on Tuberculosis. An Experimental Inhalation Study of Two Varieties of Dust: Histopathologic Observations.** *Amer. Rev. Tuberculosis.* 1958, Oct., v. 78, No. 4, 512–23, 3 figs. [19 refs.]

This experimental study is an extension of a more general enquiry already reported elsewhere [this *Bulletin*, 1959, v. 34. 57]. Tuberculosis was induced with a special strain of organism in 113 guineapigs, whose lungs were "dusted" with 2 varieties (calcium carbonate and calcium sulphate) of Fiberglas (which is a conglomerate of glass fibres (15%), polymerized polyester resin (35–60%) and either calcium carbonate or calcium sulphate fillers (25–45%)). Both dusts caused a limited, transient increase of the tuberculous infection. This increase was more marked and more prolonged in the animals exposed to the calcium carbonate variety than in those exposed to the calcium sulphate variety. The author suggests that calcium sulphate is less tuberculogenic than calcium carbonate. However, he emphasizes that this inference must be regarded with caution as the special Rl infection went through a phase of reduced virulence during the course of the experiments. *A. Meiklejohn*

MORROW, C. S. & KANTOR, M. **Silicotuberculosis. Results of Medical and Combined Medical-Surgical Therapy.** *Amer. Rev. Tuberculosis.* 1958, Oct., v. 78, No. 4, 524–35. [13 refs.]

Between September 10, 1952, and December 1, 1956, 25 hardcoal-miners suffering from bacteriologically confirmed anthraco-silico-tuberculosis were treated in the Veterans' Administration Hospital, Wilkes-Barre, Pennsylvania. None had previously received any treatment. Of the 25 patients 9 were in the age-group 50–9 and 10 in the group 60–9, with an average of approximately 30 years' employment in the mines. Treatment

consisted of chemotherapy, streptomycin, PAS and isoniazid, or chemotherapy supplemented by various surgical procedures, including lung resection. Most of the patients received streptomycin combined with isoniazid; few were treated with any other combination or with all 3 drugs.

The efficacy of treatment was measured by radiographic changes and sputum examination for *Mycobacterium tuberculosis*.

The results of chemotherapy alone (19 cases) from the standpoint of cavity closure, along with reversal of infectiousness, were poor as compared with simple tuberculosis. The results of chemotherapy and surgery (6 cases) were good, particularly in cases of lung resection.

The authors submit that if chemotherapy is to play a significant role in silico-tuberculosis, it would appear advisable to regard conglomerate disease in its initial stages as tuberculous, in the presence of a positive tuberculin test, and to treat it as such if only to prevent further conglomeration.

The article includes the case reports of 6 patients; these will be of interest to physicians who are treating similar cases. *A. Meiklejohn*

WILLIAMS, M. H., Jr. & ZOHMAN, Lenore. **A Simplified Method for Estimation of the Diffusing Capacity of the Lung in Subjects without Airway Obstruction.** *Amer. Rev. Tuberculosis.* 1958, Aug., v. 78, No. 2, 173–9, 3 figs.

One of the difficulties in estimating the overall diffusing capacity of the lung (D_{CO}) from measurements of the rate of uptake of carbon monoxide is to get a value for the mean alveolar tension of that gas (P_{ACO}) during the period of gas uptake which is observed. In one variety of the steady state method for measuring CO diffusing capacity, described by FILLEY and co-workers (*J. Clin. Investigation*, 1954, v. 33, 530), measurement of the arterial carbon dioxide tension (P_{aCO_2}) is used as a guide to the mean alveolar carbon dioxide tension (P_{ACO_2}) (which will be reasonably valid even in subjects who have inequality of ventilation within their lungs) so that this P_{aCO_2} can then be used to calculate "dead-space" and hence P_{ACO}. This paper from the Cardio-respiratory Laboratory, Grasslands Hospital, Valhalla, New York, presents data designed to show what error would be introduced when measuring the steady state D_{CO}, by simply assuming either a normal value for P_{aCO_2} or a normal value for the ratio of dead space to tidal volume (Vd/Vt) in subjects without airway obstruction.

In 21 consecutive patients referred to the laboratory who had negligible airway obstruction, as determined by their having a maximal mid-expiratory flow-rate of more than 1·0 litres per second, 3 calculations of D_{CO} were made. Measurements of CO uptake were done during estimated maximal muscular exercise for 5 minutes in the recumbent position. Then the D_{CO} was calculated (1) by using P_{aCO_2}, calculated from measured arterial carbon dioxide content and *p*H, (2) by assuming a P_{aCO_2} of 40 mm.Hg, (3) by assuming a Vd/Vt ratio of 40%, the average found in these patients. The results are expressed as a series of scatter diagrams and the authors conclude that the estimated D_{CO} agreed well with that calculated from direct measurement of arterial P_{CO_2}.

[In fact, even in these selected subjects the estimated D_{CO} is only "in most instances within 25 per cent" of the value obtained from measurement of arterial P_{CO}. The authors make the statement that in the absence of severe airway obstruction this simplified technique may help distinguish asthma from emphysema. Since they are automatically excluding many patients with these conditions and the error in the remainder may be more than ± 25%, it is difficult to see how this could be so.] *P. Hugh-Jones*

GOLDSMITH, J. R. **A Simple Test of Maximal Expiratory Flow for detecting Ventilatory Obstruction.** *Amer. Rev. Tuberculosis.* 1958, Aug., v. 78, No. 2, 180–90, 3 figs. [15 refs.]

Indirect estimation of the maximum breathing capacity from the volume exhaled in a given time during a single forced expiration has been widely used in recent years as a simple and reasonably valid test of a patient's maximum ventilation. In this paper (from the Veterans Administration Hospital, Seattle, the Department of Medicine, University of Washington Medical School and the Department of Preventive Medicine, Harvard Medical School, Boston) the author describes a simple device for measuring maximum rate of airflow itself, rather than some combination of volume and time. It consists of a rugged, vitreous, porous cup, which can be mounted on the end of a tube to act as resistance, across which the pressure drop which is proportional to air-flow, can be measured instead of using the wire-screen as in the conventional pneumotachograph. The whole apparatus is compact and robust, and it is claimed that the subject is usually unaware of resistance to expiration. The device including mouthpiece, vitreous resistor and indicating pressure gauge is called a Puffmeter.

Calibration of the Puffmeter in series with a screen pneumotachograph showed high correlation between maximum Puffmeter value and the maximum height of the recorded flow curve, not only during steady airflow but on 31 actual breaths. ($r = +0{\cdot}992$). In 233 sets of data on consecutive subjects a correlation coefficient of $r = +0{\cdot}937$ was obtained between Puffmeter readings and the maximal breathing capacity test. Data on the error of reading the instrument, variations between resistance of different porous cups, are given and the author concludes that it is a suitable instrument for clinical or screening use in detection of persons with pulmonary air-flow obstruction.

P. Hugh-Jones

SIMPSON, T. **Chronic Bronchitis and Emphysema.** *Tubercle.* 1958, Oct., v. 39, No. 5, 307–27, 7 figs. [32 refs.]

This article is a good summary of present knowledge of chronic bronchitis and emphysema as seen at a chest clinic. It is necessarily dogmatic and therefore it is easy to criticize some of the author's statements,

e.g. the suggestion that emphysema can usually be excluded by clinical methods and radiology. Useful features are a series of clinical summaries of cases illustrating the author's analyses. The paper does not claim to present original work, but as a short account of a very common, but still obscure condition, it can be strongly recommended. *F. H. Young*

LAUER, O. Das Luftstrahlsieb, ein neues Gerät für die Durchführung von Prüfsiebungen. [**The Air-Jet Sieve, a New Device for Sieve Analysis**] *Staub.* Düsseldorf. 1958, Oct. 1, v. 18, No. 10, 306–9, 16 figs.

Below the gauze of the sieve a radial slit is situated which rotates upon a central axis so that a powerful air blast emerging from it lifts the dust from each part of the gauze in turn. The air space below the sieve is exhausted through a filter. Fine dust particles, which tend to adhere to coarser ones, are dispersed and swept through the gauze to the filter.

The speed of sieving is considerably enhanced by this device and the coarse fraction is obtained quite free from particles small enough to pass through the mesh. *C. N. Davies*

PETER, F. Überblick über aktuelle Fragen der Staubbekämpfung in der Steinindustrie. [**Survey of Current Dust Suppression Problems in the Stone Industry**] *Staub.* Düsseldorf. 1958, Oct. 1, v. 18, No. 10, 301–5, 5, figs.

According to the Steinbruchs-Berufsgenossenschaft, about 28,000 persons are exposed to dust in the German stone industry. A relaxation of the conditions of compensation for silicosis was made in 1952 with the result that the number of persons newly compensated in 1953 rose to 435. The figure for 1957 was 166.

The processes involved are classified as winning (especially drilling), crushing by hand and by machine, and dressing. Current dust suppression measures applied to these processes are described; they include water sprays, suction drilling, and local extraction. It is considered that small-bore drilling (diameters under 30 mm.) is one of the most difficult processes to deal with.

Cooperation between employer and worker, and the place of physics and engineering in preventive work, are discussed. *C. N. Davies*

BOWKER, J. R. **The Liberation of Phosphine in the machining of Spheroidal Graphite Iron.** *Trans. Ass. Indust. Med. Officers.* 1958, July, v. 8, No. 2, 50–52, 3 figs. Discussion 53.

Some interesting illustrations are provided to show the form that graphitic carbon takes in cast iron. The spheroidal graphitic variety provides an increase both in tensile strength and in ductility.

One man milling spheroidal graphite iron complained of the odour and of irritation of the upper respiratory tract. The fresh dust has a smell similar to acetylene. The typical smell of this gas is due to traces of phosphine present as an impurity. Phosphorus is present in all iron in small quantities, but the suggestion that phosphine was evolved during machining was rather alarming.

However, careful analysis in the firm's research laboratories showed that 6 p.p.m. of phosphine were produced at 1 cm. from the tool point, and the concentration was reduced to 0·8 p.p.m. at 20 cm. Even if the operator held his face exceptionally close to the work these concentrations are unlikely to lead to symptoms. *T. O. Garland*

FAUTREL, M. Exploitation statistique de données biologiques sur le pré-saturnisme clinique professionnel. [**Statistical Assessment of the Biological Data on the Early Detection of Occupational Lead Poisoning**] *Arch. Malad. Professionnelles.* Paris. 1958, Jan.–Feb., v. 19, No. 1, 5–20. [10 refs.]

This article illustrates the application of statistical techniques, simple and more sophisticated, to the problem of the detection and prevention of lead poisoning in industry. For two groups of workmen, one occupationally exposed to lead, observations were made on 5 clinical measures appropriate to the study of chronic lead poisoning—red cell stippling, lead concentration in blood and urine, urinary level of coproporphyrin and blood protoporphyrin. The mean levels and the standard deviations of serial measurements on the same person in the unexposed group were then used to set physiological limits for the variation of those measures in unaffected men. The t test of STUDENT and a non-parametric test developed by MANN and WHITNEY (*Ann. Math. Stats.*, v. 18, 52) gave an indication of the clinical measures which differentiated significantly between those exposed to lead and the others. Urinary lead levels in the two groups seemed to be the only measure which differed by no more than would be reasonably attributed to chance variation.

The practical value of any one of these indices of chronic lead poisoning depends on its correlation with the others. It is pointless to duplicate measures which give substantially the same answer. The author points out that the ordinary product moment correlation coefficients may not be appropriate for the distributions concerned and suggests KENDALL'S τ coefficient based on rank orders (*Rank correlation methods*, 1948, London: Charles Griffin & Co.). By its use, he shows that in the exposed group, the results of the two types of porphyrin estimations are closely associated with each other but not with the stipple cell count. Both stipple cell count and the urinary coproporphyrin level may be used in the detection of an occupational lead hazard in groups of men. Similar methods can be applied in the medical supervision of individuals, and the author gives examples of the application in this context of some of the newer non-parametric statistical techniques. On the basis of the limited experience reported in this study, he suggests that stipple cell counts repeated at least twice, are of diagnostic value in the early detection of lead poisoning. *D. D. Reid*

ZEGLIO, P. Gli esiti a distanza del mercurialismo cronico. **[Late Results in Mercurial Poisoning]** *Rass. Med. Indust.* Turin. 1958, July–Oct., v. 27, Nos. 4/5, 427–88, 18 figs. [52 refs.]

In this report the author gives the findings 15 years after an incident in which 33 persons suffered acute Hg poisoning at Alessandria (Piedmont) in 1943. The nature of the incident is not mentioned.

Of the 33 patients only 1 was male; within 3 years all received compensation for not less than 21% disablement and 2 for 100%. 5 eventually returned to work and compensation was stopped; in 3 it was reduced, in 2 it was stopped because of death (1 was not due to Hg), in 8 it was unchanged and in 16 it was increased. In the 5 who returned to work the poisoning was slight.

In 1958 10 patients [see below] were given most thorough clinical, laboratory and X-ray examinations and the results are reported for each individual. All were among the 16 who received increased compensation.

Symptoms. Among the most prominent were marked psychomotor disturbances, patients being liable to sudden outbursts of temper for no apparent reason, headache, asthenia, melancholia, anorexia and insomnia. All complained of myoarthralgia.

Signs. Tremor was the most obvious (beautifully illustrated by photographs taken in the dark with small electric lamps fixed to the patients' fingers). The tremors varied in the most bizarre manner; they were neither exclusively static nor typically intentional and could arise without, but especially with, a stimulus. Changes in skin sensation to various stimuli with zones of hypo and anaesthesia were found, and 6 patients who had been examined by VIGLIANI in 1942 all showed diminution of sensation in 1958—which is against a purely functional origin. 5 had definite hyperthyroidism as demonstrated by ^{131}I take-up.

Auditory and vestibular system. In 9 patients examined the audiograms showed hearing loss even from 500 Hz with *sudden and complete loss* at between 6,000 and 8,000 Hz. This was not associated with age changes and seems to be the result of toxic action of Hg on the cochlear branch of the eighth nerve. 7 patients showed hypoexcitability of vestibular function and sometimes vertigo; 2 had rotatory nystagmus, while in all the Romberg was always ++.

Ocular system. By slit lamp 4 patients showed small whitish spots on the anterior and posterior surfaces of the lens which were regarded as specific metallic impregnation. No lessening of vision was found and neither fundal changes nor retrobulbar neuritis. Only 2 showed restriction of the visual fields which were not considered specific.

Serum electrophoresis showed an alteration in the albumin/globulin ratio with increased gamma globulin. The Rose-Bengal liver function test showed reduced uptake and excretion and, including the tests for colloidal lability, all 10 patients showed some signs of hepatic damage; as none was an alcoholic there was a strong suspicion, but not proof, of injury by Hg. No evidence of renal damage was found after water excretion and concentration tests.

Prognosis. Zeglio emphasizes that the outcome of Hg poisoning cannot be forecast as it varies from case to case. Patients with slight poisoning improve with the passage of time and may even recover completely if removed from their work, while those with moderate or severe poisoning, even if so removed, show an inevitable tendency to progressive worsening. Hypertonia and extrapyramidal symptoms tend to persist. Improvement in the tremors was not seen.

[Of the 10 patients thus specially examined the name of 1 does not appear as such in the list of those originally compensated, although she is stated to have had 50% disablement in 1947. A note of the treatment carried out would have been helpful, especially as regards the value (if any) of chelating agents.]

W. K. Dunscombe

HUEPER, W. C. **Experimental Studies in Metal Cancerigenesis. X. Cancerigenic Effects of Chromite Ore Roast deposited in Muscle Tissue and Pleural Cavity of Rats.** *Arch. Indust. Health.* Chicago. 1958, Oct., v. 18, No. 4, 284–91, 14 figs. [10 refs.]

"The implantation of chromite ore roast mixed with sheep fat into the pleural cavity and muscle tissue of the thigh of rats resulted after two years in the production of squamous-cell carcinomas coexisting with sarcomas of the lung in 2 of 25 rats, 4 of which survived into the cancer-bearing period, and of 3 fibrosarcomas of the thigh in 31 rats, 29 of which were alive at the appearance of the first of these tumors.

"These observations strongly suggest that chromite ore roast contains carcinogenic constituents which possibly are identical with the acid-soluble, water-insoluble chromium compounds present in chromite ore roast, exerting a sufficiently strong and prolonged effect upon exposed tissue without causing its necrosis by an acute corrosive action.

"The failure of previous experiments aimed at the production of cancers by various chromium compounds is tentatively attributed either to a release of biologically active chromium from the substances used (metallic chromium, chromite ore) in amounts insufficient for a carcinogenic response by the exposed tissue or to an excessive corrosive and necrotizing action of such materials, preventing thereby any reaction to chromium from living cells."

Addendum

"The concept of a direct causal role of chromium in the production of the cancers reported here has recently been strengthened by the observation of sarcomas in 6 of 35 rats which had received implants of 25 mg. of synthetically prepared sintered calcium chromate containing only traces of other elements. The sarcomas developed within five to six months after implantation around these chromate deposits. Twenty-seven surviving rats of this series will be kept under observation for a total period of 24 months for a possible appearance of additional cancers."

PATERNI, L. Emopatie da idrocarburi benzenici. [**Blood Dyscrasias due to Aromatic Hydrocarbons**] *Rass. Med. Indust.* Turin. 1958, July–Oct., v. 27, Nos. 4/5, 335–426, figs. 1–21 & 33–46 (9 coloured on 4 pls.) [Numerous refs.]

This paper, which is almost a monograph, was given to the 22nd Italian National Congress of Industrial Medicine in September 1958, and is supported by animal experiments and by reports on 18 patients.

Benzene and its higher homologues, such as toluene, xylene, etc., and their derivatives, play an immense and continually increasing part in industry. The rubber, rotogravure and spray-painting industries furnish the majority of patients.

As regards the metabolism of benzene in the body, the most important portion is that which becomes partially oxidized to phenol and diphenols. In acute poisoning the homologues are more toxic than benzol, but it is quite the reverse in chronic poisoning.

Symptomatology. In benzolaemia the action is very largely on the blood and blood-forming organs, but individual predisposition and deficient resistance of the haemopoietic system are definite predisposing factors. In the 18 cases studied the most frequent symptoms were asthenia, headache, anorexia, vertigo and slight fever. No organic nervous disease was found, but paraesthesiae of the limbs and muscular pains, while not common, were of considerable diagnostic value. Haemorrhages were seen in 8 patients and retinal haemorrhages were relatively frequent.

Action on (1) The blood. The erythrocytes may not be deficient for a considerable part of the illness and immature erythrocytes are not common. There may be an increased mean corpuscular volume (MCV) and a shift to the right of the Price-Jones curve. The free erythrocyte protoporphyrin IX may be considerably increased in grave cases. Leucocytosis may occur in the initial phase, but leucopenia is part of the pancytopenia in the main stage; the granulocytes are more affected than the lymphocytes. Immature leucocytes are rare. Thrombocytopenia is usually early and important, but there seems to be no relationship between their lack and any change in platelet function. There is a marked increase in serum Fe. Coagulation time (Howell) is prolonged, although it varies only slightly in Quick's test. There is slight diminution of fibrinogen and in some cases reduced clot retraction. (2) Bone-marrow. The changes can be of 3 types according to whether there is aplasia, hyperplasia or hypoplasia of the mesenchymal or parenchymal cells. There may be a combination with disturbance of maturation affecting especially the "blast" cells. Usually the haemoblastosis remains localized to the marrow, but if cells with these characteristics enter the blood the prognosis is bad. The spleen shows marked Fe deposition. In toluene and xylene poisoning the marrow is usually aplastic but this is not a constant feature.

Course and Prognosis. There may be acute or latent benzolism or late benzhaemopathy. In many cases with only slow improvement myelograms may show persistent myelopathy; the blood cells are restored only slowly. The prognosis must be guarded in all cases where the tendency to resolution is slow but is good in poisoning by the higher homologues. Haemoblasts in the peripheral blood mean a grave outlook.

Diagnosis. There must be a complete examination of both the cellular and fluid elements of the blood together with repeated myelograms. Urine testing to determine the proportion of inorganic to total sulphates, and so the organic sulphates, may be valuable, and also the ascorbic acid loading test. Paraesthesiae of the limbs may be a valuable symptom.

Pathogenesis. Points especially emphasized are that individual predisposition, and poisoning by small doses repeated at intervals over long periods, are particularly important. In all cases where myelopathy occurs there is also an action on the spleen; haemoblastosis is always preceded by marrow aplasia. Haemolysis is neither a constant nor an essential pathogenetic factor.

Treatment. In addition to the usual measures, transfusions may be given although care must be taken to see that the natural stimulus to the medulla is not reduced. Vitamins B and C are not of much use but corticotrophin is of definite value. It should be given in doses of 100–150 mgm. daily. Splenectomy is of doubtful or little use.

Prevention. The prime importance of the replacement wherever possible of benzene by its higher homologues is particularly stressed. Unfortunately improvement in preventive measures has not run parallel to the increased industrial use of this substance. Finally, Paterni demands legislative provisions to ensure that there is the most scrupulous application of all the known preventive measures in those industries where known risks exist. *W. K. Dunscombe*

SAITA, G. & MOREO, L. Porfirine libere eritrocitarie, coproporfirinuria, sideremia in un caso di solfoemoglobinemia da intossicazione acuta da nitroclorobenzolo. [**Free Erythrocytic Porphyrins, Coproporphyrinuria and Sideraemia in a Case of Sulphohemoglobinemia due to Acute Nitrochlorobenzol Poisoning**] *Med. d. Lavoro.* 1958, Aug.–Sept., v. 49, Nos. 8/9, 494–503, 1 graph. [21 refs.] English summary.

The authors point out that the formation of porphyrin is closely related to the synthesis of Hb, hence the renewed interest in the porphyrin exchange in conditions causing methaemoglobinaemia or carboxyhaemoglobinaemia. Sulphohaemoglobinaemia is rare because several factors are necessary for its manifestation, but the nitrate derivatives of benzol are the most likely; it has been found after acetanilide, phenacetin or sulphonamide treatment and may be more common than suspected, as the nitrated benzols which catalyze the formation of sulphahaemoglobin have also an oxidizing and methaemoglobinizing action.

The authors report the case of a 25-year-old male who supervised machines which prepared nitrochlorobenzol by nitrating chlorobenzol by nitric and sulphuric acids, forming a mixture of ortho- and para-nitrochlorobenzol. One afternoon about 50 kgm. of the mixture overflowed on to the floor and the worker, without protection, cleared it up. The next morning he had slight headache and noticed his face was bluish,

but continued working for 2 days. Then the headache became severe and there was intense cyanosis even to the finger tips. On admission to hospital blood spectroscopy showed both sulphaemoglobin and methaemoglobin 35%. These gradually diminished, but sulphaemoglobin was still present 8·5% on discharge 24 days later. Numerous tests for haemopoiesis and of blood function and components were carried out. A few days after admission both blood coproporphyrin and protoporphyrin had increased, gradually diminishing until the coproporphyrin disappeared completely. The blood Fe, which also was increased, eventually returned to normal levels. There was a reticulocyte crisis on the 9–11th days and the reticulocyte and blood protoporphyrin curves agreed very well. Evidence of haemolysis was amply proved by, among other signs, the hypererythroblastic activity of the bone marrow and the increase in blood Fe. Very numerous Heinz bodies were seen at the height of the illness, but gradually disappeared. They never appear in pure sulphaemoglobinaemia but, as in this case, can occur when the condition is due to poisons which, at the same time as producing sulphaemoglobin also cause degradation of the Hb molecule.

The authors discuss how the sulphaemoglobin came to be formed and mention the possibility that, as H_2SO_4 was used in the preparation, sulphurous compounds may have formed and have been inhaled. They consider that sulphohaemoglobinaemia *per se* does not cause any change in the free erythrocyte porphyrin or the coproporphyrin, and that it was not the cause of the rapid haemolysis and anaemia.

W. K. Dunscombe

WIDMANN, H. Akutes Nierenversagen und Tetrachlorkohlenstoffvergiftung. [**Acute Renal Failure due to Carbon Tetrachloride Poisoning**] *Deut. med. Woch.* 1958, Sept., 12, v. 83, No. 37, 1611–12, 1615–18, 1639, 1 fig. [26 refs.]

As introduction to an account of a case of carbon tetrachloride poisoning the literature on the toxicity of CCl_4 is reviewed with emphasis on the rapidity with which it may have poisonous effects on inhalation of small amounts and on the frequency of renal damage as one of these effects.

A pharmacist aged 37 years, who was well aware of the dangers of carbon tetrachloride, undertook to clean the floor of his shop in the afternoon with a mixture of 90% carbon tetrachloride, 5% butyl acetate, 3% amyl acetate and 2% chloroform. He used about 500 ml. of this mixture in his task, which he performed in a kneeling position while doors and windows were kept open. When he got up after about 15 minutes he felt as though intoxicated but improved after 10 minutes yet had feelings of oppression in the head and nausea which persisted and had got much worse by the next morning. He then had attacks of giddiness, vomiting and weakness of the legs and the temperature rose. About 25 hours after the inhalation of the carbon tetrachloride the family doctor observed yellow staining of the sclerotics. The patient was later admitted to hospital as by this time there was severe pain in both renal regions and no urine had been passed for 24 hours. There is a full description of the clinical findings and the results of laboratory investigations throughout the course of the illness which was one of renal failure and of hepatic involvement. A figure sets out the results of analysis of the urine for urea and creatinine, the alkali reserve and the blood pressure for a period of over 30 days. In another table are some particulars of electrolytes in the serum and of the blood picture.

The patient recovered and was discharged from hospital on the 57th day of his illness. At a follow-up examination after 8 months his condition was satisfactory although he had some shortness of breath on exertion and the electrocardiogram showed the signs of a persisting left-sided involvement. *M. E. Delafield*

WILLIAMS, H. I. **Carbon Dioxide Poisoning. Report of Eight Cases, with Two Deaths.** *Brit. Med. J.* 1958, Oct. 25, 1012–14.

"Although rarely reported, carbon dioxide poisoning is probably not so infrequent an occurrence" is the statement, based on some of the literature on the subject, which introduces an account of the carbon dioxide poisoning of 8 persons from the handling of a ship's cargo. A liner arrived at Penang with a cargo of onions and a quantity of "jaggery" (a crude sugar from palm tree sap). A hold laden to within 9 feet of the deck was opened. A labourer entered and collapsed as he was standing on the onions. Another man went in to help him and also collapsed. Then the ship's doctor and a ship's officer went to their aid and the doctor collapsed as he was lifting the first unconscious man. 1 of the ship's crew who went in to assist was also overcome. With the help of breathing apparatus the 4 poisoned men were then brought out and were taken to hospital when 2 of them were found to be dead. 4 labourers who had entered the hold for short periods developed minor symptoms. Estimates of the length of time that the men were lying unconscious in the hold varied considerably but seemed to be 5 minutes in the case of the doctor and about 15 minutes in the others. The first patient on admission was deeply comatose and was having continuous convulsions but was not cyanosed. He recovered consciousness in about 7 hours and was discharged after 8 days. The doctor was conscious on admission and recovered rapidly. Neither he nor the 4 other patients with minor symptoms showed any cyanosis. No post-mortem on the 2 dead men was done because the relatives objected but the bodies showed cyanosis of the finger nail and toenail beds and of the buccal mucosa.

Analyses of the gases of the holds were performed (no numerical results are given) and "appreciable reaction for carbon dioxide" was obtained in the opened hold and strong reaction in the unopened holds. Laboratory experiment showed that in a sealed flask one-third filled with onions the concentration of CO_2 in the air after 5 days was over 30%.

The toxic action of carbon dioxide is discussed with mention of a number of published reports of incidents of poisoning by this gas. *M. E. Delafield*

FLOYD, E. P. & STOKINGER, H. E. **Toxicity Studies of Certain Organic Peroxides and Hydroperoxides.** *Amer. Indust. Hyg. Ass. J.* 1958, June, v. 19, No. 3, 205–12. [19 refs.]

Organic peroxides are likely constituents of certain types of oxidizing smog and important as industrial catalysts, intermediates and raw materials for synthesis. Many of them are abundant sources of free radicals. For these reasons the authors have conducted tests in their laboratory to determine the toxicity of these compounds on small mammals. The peroxides used were di-t-butyl peroxide, t-butyl hydroperoxide, cumene hydroperoxide and methyl-ethyl-ketone peroxide, and their characteristics are described in 2 tables. Because the conventional chemical methods (iodide or stannous chloride) are not specific for organic peroxides, whereas the polarographic method distinguishes between peroxides and hydroperoxides and is specific for determining both, this method was selected as the most desirable for this study in which mixtures of compounds were involved. The rats used in these experiments were Wistar-derived adult male albinos, weighing approximately 200 gm. at the beginning of each test. The mice were Swiss derived adult male albinos, having an initial average weight of 20 gm. each. The rabbits were white males of the New Zealand strain weighing from 2·7 to 6·5 kgm. The original should be consulted for full details concerning the experimental methods and the results.

It was found that the hydroperoxide was far more toxic than its dimeric peroxide, by all routes of administration. All the compounds tested were skin and eye irritants, except di-t-butyl peroxide, and cumene hydroperoxide proved to be extremely irritating to rabbit eyes. Of the 4 compounds studied methyl-ethyl-ketone peroxide was the most toxic by all 5 routes of administration (oral, intraperitoneal, inhalation, application to the skin and eye). Di-t-butyl peroxide was the least toxic and is classed as "relatively harmless" to "slightly toxic" (inhalation). One possible correlation between the degree of toxicity and the properties of these compounds may be found in the polarographic half-wave potential, $E_{\frac{1}{2}}$. Di-t-butyl peroxide, the least toxic of the group, was not reduced by the polarographic technique, where the other organic peroxides, t-butyl hydroperoxide, methyl-ethyl-ketone peroxide and cumene hydroperoxide, which as a group are "moderately toxic" compounds, have comparable half-wave potentials (−0·92 to −1·09 volts). Histopathological study failed to reveal any site of damage, although there were questionable indications that the liver may be involved. It was demonstrated in rats for at least 3 of the 4 organic peroxides tested that repeated sublethal doses (1/5 LD50) either orally or intraperitoneally resulted in cumulative effects, ending in death of some of the animals. Di-t-butyl peroxide did not show cumulative toxicity intraperitoneally and t-butyl hydroperoxide, none orally.

Some protection from lethal doses of hydrogen peroxide was demonstrated in rats following exposure to cumene hydroperoxide and subsequent challenging with hydrogen peroxide vapours.

P. J. R. Challen

SPECK, Louise B. & MAASKE, C. A. **The Effects of Chronic and Acute Exposure of Rats to Endrin.** *Arch. Indust. Health.* Chicago. 1958, Sept., v. 18, No. 3, 268–72, 3 figs.

Endrin, a chlorinated hydrocarbon insecticide, is said to produce electro-encephalographic (EEG) changes. These studies on rats were designed to investigate how far these changes can be used as an indication of toxic exposure and whether the EEG returns to normal after exposure ceases.

Details are given of the rats' diet, the dosage of endrin, and the technique of recording the EEG, together with autopsy findings after lethal doses and after smaller doses producing chronic changes.

EEG recordings after highly toxic doses showed irregular slowing, irregular spikes and frequent convulsive discharges which were apt to be set off by auditory stimuli or touch. The EEG changes were minimal in those receiving doses producing chronic symptoms only, such changes as were evident being most marked in the early stages of exposure.

The conclusion reached, therefore, is that the EEG is not a useful index of toxicity except after an acutely toxic exposure and in the initial stage of a lesser exposure.

T. O. Garland

J. AMER. MED. ASS. 1958, July 26 & Aug. 30, v. 167, Nos. 13 & 18, 1636–7; 2203–5. **Occupational Dermatoses. (i) An Introduction.** [Report prepared by the Committee on Occupational Dermatoses (BIRMINGHAM, D. J., Chairman) of the Council on Industrial Health, American Medical Association (HOLLAND, B. D., Secretary).] **(ii) Predisposing and Direct Causes.**

This is the work of a committee. It contains nothing new and merely constitutes a rationalization of current opinion based on the face values of published statistics relating to occupational dermatoses and on speculations founded on theoretical notions of the reactions of the skin to noxae.

We are told that the rising morbidity is mainly due to the increasing variety and chemical complexity of industrial contacts and that casualties occur merely because of the imperfect defences of the human skin, inadequate protection by special clothing and barrier creams, carelessness or inexperience in their use, neglect of ablutions, or activities outside of the work environment.

The failure of the skin to recover from industrial injury (as it is well known to recover after accidental injury by cosmetics, articles of personal adornment, horticultural hazards, therapeutic adventures and the like) is tentatively attributed to overtreatment. We are told that in the personal experience of members of the committee some 30–40% of their own cases are ultimately determined to be non-occupational in origin. The part played by individual susceptibility is not denied; but emphasis is placed rather on tangible factors, such as complexion, pigment, sebaceous activity, sweating and the pre-existence of manifest dermatoses, rather than on the widespread disease-proneness, and morbid consciousness of the possibilities of disease,

that have so far frustrated all the efforts (to keep us well) of a progressive medical science.

The fact that dermatoses, considered by this committee to be easily preventable, constitute anything from 30% to 60% of all occupational diseases reported, and cost more than $100,000,000, perhaps even $200,000,000 a year, would seem a strong incentive to realistic study of the somatic reactions of mankind to the increasing complexities of life rather than the occasion for pronouncements implying the usefulness of a naïve and mechanistic approach to this difficult subject. *J. H. Twiston Davies*

SMITH, D. A. **Industrial Skin Disease—Prescribed Disease (P.D.) 24b.** *Trans. Ass. Indust. Med. Officers.* 1958, July, v. 8, No. 2, 79–80.

The author discusses a series of 40 cases certified by him as P.D.24B [now P.D.42 (dermatitis)] during 6 months.

He finds that "in most cases the cause is clear and unequivocal". But he would not accept as 24B a "purely contact or allergic dermatitis"; and as an example he quotes a case of allergy to the material forming the face piece of a pair of welding goggles. On the other hand he would regard the development of an eczematoid dermatitis of the legs in a man subject to seborrhoea or having "tinea of the feet" as fully attributable to "conditions unduly dusty or wet".

Pit water, we learn, "is acid and contaminated with coal dust". [But the horny layer is well known to be highly tolerant of acid; lotions and creams designed to restore the "acid mantle" are widely advertised. Coal tar has had for so long a high reputation in the treatment of infantile facial eczema that it is even surprising that nobody has offered us a shake-lotion of coal dust! One could imagine that the composition of pit water must vary with geological conditions, the use of calcium chloride, and the presence of pit ponies and rats, but it must inevitably contain sodium chloride, and surgeons, whether or not they know that it prevents maceration, are always careful to add salt to the water when using rubber gloves wet.]

J. H. Twiston Davies

MOLLOY, C. C. **A Survey of Skin Disease in a Group of Factory Workers.** *Trans. Ass. Indust. Med. Officers.* 1958, July, v. 8, No. 2, 54–60, 1 fig. Discussion 60.

Any systematic clinical study of skin disease is welcome even though the period of observation, 130 days which moreover included an epidemic, is rather too much less than a year to make the figures acceptable. But the design of the experiment is exemplary, the information derived from it of considerable interest, and we keenly look forward to the further instalments promised.

The author, while emphasizing the differences in clinical opportunity between the industrial medical officer and dermatologist, admits that after a time personnel become reluctant to report for fear of being examined and asked a lot of questions [and it might well be that the smell of compensation could account for some of the difference in morbidity rates between industrial (13% and 145 cases) and non-industrial (3% and 10 cases) personnel]. These rates are high as compared with prewar *viz.* about 1% without special hazard (*e.g.* chrome turpentine and rubber) and 3% with. It is noteworthy not only that 3 times as many females as males were affected but 20 times as many females between 16 and 25 as males of the same age group.

The classification of industrial workers according to the degree of exposure is useful, but the incidence in "those who worked in groups where tetryl, etc., were handled but who were not themselves in close contact" being so much lower than in the rest of the factory population leaves one to wonder if they were not also distinguished by some other factor, perhaps economic or social. The number of non-industrial cases is far too small to be used in any kind of comparison.

Of the 150 cases only 35 were considered to be of contact dermatitis but, presumably partly because for administrative purposes all skin disease in wage earners tends to be regarded as occupational and partly because of inadequate numbers, the very interesting breakdown that follows ignores this factor. That 69% of cases recovered completely does indeed suggest that the series included a high proportion of cases attributable to contact with irritants but it is hardly justifiable to equate recovery with "result of treatment" or to attribute delay in seeking treatment to anything but familiarity with skin trouble and disillusionment. Although personnel had been carefully selected before employment on a basis of no previous skin disease no less than 70% of the 150 subsequently admitted earlier attacks.

Another feature of this series suggestive of the important part played by volatile external irritants is that among exposed personnel, as opposed to non-exposed, 7 times as many had lesions on the face without involvement of hands. Many non-dermatological observers are apt to ignore the relative impermeability of the horny layer of the palms and tend to include the very common constitutional patchy eczema of the extremities among their cases of industrial dermatitis. *J. H. Twiston Davies*

KNIGHT, A. L. **Dermatitis. A Report on the Five-and-One-Half-Year Experience of an Ammunition Plant.** *Arch. Indust. Health.* Chicago. 1958, Aug., v. 18, No. 2, 155–67, 11 figs. [12 refs.]

"The five-and-one-half-year experience of an ammunition plant with 1,566 dermatitis cases is reported. A substantial case rate decrease occurred during the survey period. The decline in dermatitis was similar to the decline in the over-all occupational sickness and accident rate.

"Graphs show the yearly dermatitis rates, the relationship to total employment, summer dermatitis increase, the diagnostic categories, and the occupational percentage of various dermatitis conditions.

"Several nonoccupational dermatitis diseases are shown to be commoner in the toxically exposed workers. Some explanations are discussed.

"The number and types of treatment rendered are summarized.

"Discussion of the reduction in the dermatitis incidence involves these topics: (1) preemployment examination; (2) annual examination; (3) job change examination; (4) monthly toxic checks; (5) return to work control; (6) treatment of sick and injured; (7) direct education; (8) indirect education; (9) aids to cleanliness; (10) environmental control; (11) protective equipment; (12) materials handling."

SCHMIDT, W. & BOSLET, W. Zur Kenntnis bleibender Hautveränderungen bei Chlorakne-Kranken-mit versicherungsrechtlichen Hinweisen. [**Studies on Persistent Skin Changes in Patients suffering from Chloric Acne—with Comments on Insurance Laws**] *Berufsdermatosen.* Aulendorf. 1956, May, v. 4, Nos. 3, 109–23, 6 figs. on 4 pls. [12 refs.]

SCHNEIDER, W. & TRONNIER, H. Über die Lichtschutzwirkung von Estern und Amiden der p-Methoxyzimtsäure im praktischen Expositionsversuch im Engadin. [**The Protective Action against Real Sunlight of Esters and Amides of p-Methoxycinnamic Acid**] *Berufsdermatosen.* Aulendorf. 1958, Aug., v. 6, No. 4, 199–206, 5 coloured figs. on pl. [20 refs.]

The experiment here described employs the method of simultaneous paired comparison in a biological assay of the protection given by certain sunscreens against natural sunshine in the Engadine.

The skin in the lumbar region was exposed for 1¼ or 2 hours to strong sunshine, neither the season, time of day, temperature nor age, sex or degree of accustomance of the subjects, being specified. A paper template about 16″ × 8″ having 8 holes 2″ in diameter covered part of the area, the skin exposed by the holes having been pretreated with the drugs named in the title in aqueous solution cream and aerosol, with a couple of unnamed proprietary preparations for comparison and 3 left untreated for control. While the superiority of the non-greasy aerosol, established by previous experiments with artificial light, was maintained it is obvious that, while it may be possible to prevent a painful erythema with these preparations, nothing short of a really opaque paste can give full protection at any rate from the pigment-provoking action of the sun. *J. H. Twiston Davies*

BARKOW, D. Zur Abgrenzung des Einsatzes von Silikonölhaltigen Hautschutzsalben. [**A Contra-Indication to the Use of Barrier Creams containing Silicones**] *Berufsdermatosen.* Aulendorf. 1958, Aug., v. 6, No. 4, 225–9, 4 coloured figs.

Whatever be the dermatological advantages of barrier creams containing silicones they must not be used where polished metal surfaces have to be protected by varnishing, because they result in varnishing defects round the fingerprints, and it is likely that similar considerations would apply to electroplating.

Polished sheets of stainless steel were cleaned with trichlorethylene and the fingerprints obtained upon them of subjects who had applied to their hands a protective inunction of vaseline, various creams with water-in-oil glycerin and stearate bases, with and without silicone. They were then sprayed with an ordinary cellulose nitrate varnish and the results colour-photographed 16 hours later.

The illustrations show that neither vaseline nor any of the preparations that contained silicones are suitable in this kind of work. *J. H. Twiston Davies*

WEITGASSER, H. Über dermatologische Einstellungsuntersuchungen als Prophylaxe beruflicher Hauterkrankugen. [**The Prevention of Industrial Dermatitis by Pre-Employment Dermatological Examinations**] *Berufsdermatosen.* Aulendorf. 1958, Aug., v. 6, No. 4, 192–9, 2 figs.

While the number, 700 or so, of new patients with eczematoid dermatitis appearing each year in the author's clinic hardly changes, the percentage of cases attributed to external irritants, in particular to irritants encountered in the course of employment, has risen, and in the case of women doubled, in the last 9 years. The author has also noted an increasing tendency for the disease to develop within a short time of starting a job, and it has occurred to him that something might be done by means of an attempt to discover and exclude from certain jobs subjects with unduly vulnerable skins. Without adducing any evidence he assumes that icthyosis, the tendency to seborrhoea, and of course the presence of manifest eczema, predispose to allergic sensitization or intolerance of maceration or degreasing. He also attaches importance to alkali tolerance tests, estimations of the lipoid and its regeneration in the horny layer and to patch tests not only with the materials to be handled but also with common allergens at threshold concentrations. He would even search for septic foci, but he attaches the greatest importance to taking a detailed history of previous employment, domestic work and hobbies. Previous exposure to cement for example would render suspect a candidate for chromium plating work and a woman who undertook much laundry work or cleaning in her spare time might well be unsuitable for work in a hairdresser's shop.

The author has been working on these lines for only 3 years and can tell us about no more than 117 cases; so quite apart from the relevance of his figures one may reasonably doubt if the numbers or the variety of his experience justify any conclusion. The problem seems to be very like that of the soldier with flat feet: should he have a field marshal's baton in his knapsack it is unlikely that they will interfere with his marching. *J. H. Twiston Davies*

BULL. SCHWEITZ. AKAD. MED. WISS. 1958, Sept., v. 14, Nos. 5/6, 297–621, numerous figs. [Numerous refs.] **Symposium on Noxious Effects of Low Level Radiation. Physical Elements and Biological Aspects.** Lausanne, 27–29 March 1958.

The 2 main sections of this symposium deal with Radioactive Fallout and Natural Sources of Radiation

(*re* hazard) and Biological Effects of Low Level Radiation. If reference is here made only to the original papers it is because space does not allow the inclusion of any comment upon the excellent discussions which follow these papers.

Radioactive Fallout by Willard F. LIBBY, p. 309, is an authoritative survey of the sequelae to atomic weapon tests, whether these are carried out in air, in water, on the ground and now underground. These last-named have far-reaching potentials and already those engaged in big earth undertakings are making use of the earth-shattering effects of underground nuclear devices. One test is described in these words: "Apparently the bomb, which had the power of 1,700 tons of ordinary chemical explosive, blew itself a bubble of vaporized rock about 55 feet in radius, which had a skin about 3 or 4 inches thick." The article lists 6 possible non-military applications of nuclear explosions.

A Survey of British Work on Radioactive Fallout by W. G. MARLEY, p. 348, deals with the tests on fission products in the air of the U.K. since 1948 and in the rainfall since 1951. A detailed study was made of the fate of the long-lived isotopes ^{90}Sr and ^{137}Cs in human food chains involving measurements on soil, grass, animal bones, milk and foodstuffs in relation to the amount of stable calcium present in the foodstuff and also in the whole diet and, in some instances, to the stable strontium content.

Dose de rayonnement admissible et doses reçues dans l'ambiance moderne [*Admissible Level of Radiation and Doses received in the Modern Environment*] by G. JOYET, p. 367. The important point here made, on the basis of elaborate measurements, is that if we are concerned about the biological effects of small doses of radiation (in the sense accepted in connexion with man's environment) then it is not upon the generation at present exposed but entirely on future generations through genetic action that these effects will be shown.

The World-wide Deposition of Long-Lived Fission Products from Nuclear Test Explosions by N. G. STEWART, p. 407. The fission products of most importance to the public health are ^{89}Sr, ^{90}Sr and ^{137}Cs. Their deposition after nuclear test explosions has been quantitatively assessed in various parts of the world. Most of the ^{90}Sr deposited is derived from those nuclear explosions whose clouds enter the stratosphere and return to earth slowly over a number of years; the fallout is proportional to the rainfall. There appears to be a pronounced maximum of this strontium in the middle latitudes of the northern hemisphere.

World-wide Distribution of Strontium-90 and its Uptake in Man by J. L. KULP, p. 420. The objective here is to be able to predict the average ^{90}Sr content and the nature of the distribution around this average for any segment of the world population at any time in the future, given a certain pattern of nuclear testing. By this means better methods are expected by the author for the evaluation of potential hazards due to ^{90}Sr. The work would seem to have a high significance, as nuclear testing is likely to continue for a long time, apart from any military aspect.

Entry of Radioactive Fallout into the Biosphere and Man by W. LANGHAM and E. C. ANDERSON, p. 434. Discussion centres round the rival theories proposed concerning the world air distribution of fission products, and there are many accumulated data on this important question.

Somatic Effects of low-intensity Radiation at different Levels of biological Organisation by A. HOLLAENDER, p. 487. This is a summary by the author of a paper later in the series, p. 611.

Le problème de l'activité biologique des faibles doses de radiations ionisantes [*The Problem of the Biological Activity of Weak Doses of Ionizing Radiations*] by H. MARCOVICH, p. 491. Weak doses can be defined not only by their absolute value, but by the degree of effect which they produce. Lysogenic bacteria are found by the author to be very radio-sensitive and by a beautifully precise experimental method he shows by their reactions a sensitiveness to doses much smaller than usually associated with biological action.

Spätschäden bei chronischer Strahlenbelastung [*Late Damage from Chronic Irradiation*] by O. HUG, p 501. The author stresses the differences in local and generalized immediate damage to cellular tissue.

Die Beurteilung genetischer Schäden durch Strahlenquellen innerhalb und ausserhalb des Organismus, [*Review of Genetic Damage from Radiation Within and Outside the Organism*] by H. MARQUARDT, p. 521. At present there are 2 mutation phenomena which, according to the author, are too little considered: the chemically caused change in hereditary material and the somatic-genetic effects.

Abhängigkeit der genetischen Strahlenschädigungen von Milieufaktoren und Strahlenqualität (*Schätzung der genetischen Strahlengefährdung des Menschen durch radioaktive Isotope*) [*Dependence of Genetic Radiation Damage on Milieu Factors and on the Quality of the Rays*] by H. FRITZ- NIGGLI, p. 550. The mutation rate is dependent upon the age of the irradiated germ cells and upon different milieu factors before, during and after the irradiation and upon the quality of the rays. A change in the gas content of the milieu can reduce the mutation rate by a factor 8. There is a plea for greater specification of detail in genetic studies.

Les effets génétiques chez l'homme des radiations ionisantes [*Genetic Effects of Ionizing Radiations in Man*] by R. TURPIN, J. LEJEUNE and M. O. RETHORÉ, p. 571. The authors have compared quantitatively the effects of natural mutations with those purposely induced by radiation, and they stress the difficulty of assessing the importance of the latter on hereditary illnesses.

Epidemiological Studies of Radiation Leukaemogenesis in Man, with Particular Reference to the Possible Nature of Dose-Response Relationship by K. M. C. BROWN, p. 580. The sources of information on this subject are reviewed, particular attention being paid to the possible association between the radiation dose and the incidence of leukaemia; the position is maintained that man is susceptible to the induction of leukaemia following exposure to nuclear and allied radiations.

S. Russ

Sanitation

WATER

(Including the Bacteriology of Water Supplies)

BUTTIAUX, R. Les streptocoques fécaux dans les eaux d'alimentation. Recherche. Espèces rencontrées. Signification. [**Faecal Streptococci in Drinking-Water. Demonstration. Species found. Significance**] *Ann. Inst. Pasteur.* 1958, Aug., v. 95, No. 2, 142–8. [26 refs.]

The author applied the technique of LITSKY *et al.* [this *Bulletin*, 1953, v. 28, 1077] for the isolation of faecal streptococci from drinking water. This method involves the incubation of the water in Rothe's medium and confirmation of the cultures produced on the same medium with the addition of ethyl violet.

He found that the technique increased significantly the proportion of contaminated waters from which faecal streptococci could be isolated. These organisms were isolated from 96 samples, whereas the Hajna and Perry method produced only 62 isolations.

It was concluded that the presence of faecal streptococci as demonstrated by the Litsky technique is a sensitive test for obtaining evidence of faecal contamination. This sensitivity is higher than that for *Clostridium welchii* and for faecal phages, but is lower than that for *Escherichia coli*. *E. Windle Taylor*

Food and Nutrition

FOOD POISONING

MACHAY-SCOLLAY, E. M. **Two Cases of Botulism.** *J. Path. & Bact.* 1958, Apr., v. 75, No. 2, 482–5.

The 2 young adults involved were members of one family and the onset was on July 21, 1955. The symptoms were of the usual type with marked loss of speech, diplopia and loss of accommodation. Both recovered in hospital after receiving large doses of botulinum antitoxin (pooled types A and B).

The food involved was a preserved fish dish prepared in Mauritius and brought privately to 1 of the victims in London. The fish used was one locally known as *Barois*, and the methods of preparation used in the island are described. After preparation, which apparently involved heating not much above 100°C., the fish mixture was poured into jars and sealed down and kept for several days. No cases of botulism have been reported in Mauritius and the toxicity of the food seems to be associated with the onions and spices used in preservation, and with the considerable period which elapsed before consumption.

Clostridium botulinum type A was isolated from the vomit of 1 of the patients and from the remains of the food eaten by both. Guineapig inoculations confirmed that the intoxication was due to *Cl. botulinum* type A. Inoculations with food extracts of varying strength, into a series of mice, suggested that each patient must have received $2{\cdot}7 \times 10^5$ LD50 (mouse) units of toxin. A sample of the food contained 2,700 mouse LD50 of toxin per gm.

Considerable difficulty was experienced in the isolation of the *Cl. botulinum* and the account of the methods used is instructive and useful.

The author points out that this is the first case of botulism to occur for 20 years in Britain.

W. G. Savage

DEMARCHI, J., MOURGUES, C., ORIO, J. & PRÉVOT, A. R. Existence du botulisme humain de type D. [**Botulism in Man caused by** *Clostridium botulinum*, **Type D**] *Bull. Acad. Nat. Méd.* 1958, v. 142, Nos. 21/22, 580–82.

The authors have investigated a small outbreak of botulism occurring in the neighbourhood of Lake Chad in January of this year. 8 Europeans belonging to 4 separate households had eaten the same salt ham *hors d'oeuvre*. 6 of these people were ill with vomiting within 10 hours of the meal and 2 of these showed nervous symptoms. One had a defect of oculomotor control for 10 days and the last, who had consumed a large amount of the ham and who had not vomited to any extent, presented the full symptoms of botulism but eventually recovered after a month.

A very powerful toxin was obtained from the meat concerned, both in the Pasteur Institute in Brazzaville and in Paris, and rigorous tests on mice protected with antiserum made it clear that this was a D type infection.

This is claimed to be the first record of disease in man caused by *Cl. botulinum* of D type.

J. W. McLeod

DOLMAN, C. E. **Type E (Fish-Borne) Botulism: a Review.** *Japanese J. Med. Sci. & Biol.* 1957, Dec., v. 10, No. 6, 383–95. [29 refs.]

DOLMAN, C. E. **Human Botulism and Staphylococcal Food Poisoning: a Review.** *Japanese J. Med. Sci. & Biol.* 1957, Dec., v. 10, No. 6, 373–81. [24 refs.]

BANNER, A. H. & BOROUGHS, H. **Observations on Toxins of Poisonous Fishes.** *Proc. Soc. Exper. Biol. & Med.* 1958, Aug.–Sept., v. 98, No. 4, 776–8.

The fresh flesh of certain fishes from particular areas of the tropical Pacific, including the puffers (*Tetraodon*) and the snappers (*Lutjanus*) is known to be essentially toxic. The object of the tests described in this paper was " to explore the nature of the toxins sufficiently to permit planning of future studies on poisoning characterized by HALSTEAD as *Ciguatera*" [this *Bulletin*, 1954, v. 29, 649]. The experiments which were undertaken are described. The test animal used was the imported mongoose which was chosen as cats were not readily available. Both types of animal show a response to the fish toxin which parallels that found in man. The toxic nervous symptoms and signs in the mongoose are described. Extracts of the fish were made in different ways and tested for their toxicity and if toxic for the stability of the toxin. The chief conclusions are that the toxin is not water-soluble but is soluble in 90% ethanol and in certain other solvents. The toxin may be detoxified when concentrated in normal atmospheric oxygen but remains toxic under nitrogen. The test previously used to assess the toxicity is not sufficiently sensitive and depends upon the suspended matter in the extracts. *M. E. Delafield*

Bacteriology and Immunity

Abstracts of papers relating to the bacteriology of plague, cholera, yaws, leprosy and certain other tropical bacterial diseases; of the rickettsial fevers; and of yellow fever, dengue, rabies and certain other tropical virus infections, are published in the TROPICAL DISEASES BULLETIN. *Their titles and page references are cited below in the appropriate sub-division of this section*

GENERAL

HAENEL, H., FELDHEIM, Gisela & MÜLLER-BEUTHOW, W. Zur mikrobiologischen Ökologie des Menschen. [**The Ecology of the Human Microbial Flora**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 172, Nos. 1/2, 73–92, 10 figs. [43 refs.]

The purpose of this communication is to determine the chief groups of microbial forms occurring as the normal flora at various sites in the human body and to estimate their relative numbers. The mouth, the intestine, the vagina, the cerumen and a variety of skin surfaces were investigated.

The method adopted was to compare the numbers of bacteria as determined:—(a) in an optimal medium suitable for growth of many different forms, and (b) those growing in a wide range of special media appropriate to separate groups.

The optimal general medium is that described by 2 of the authors (*Zent. f. Bakt.*, I. Abt. Orig., 1957, v. 169, 196). Special media for lactobacilli, *Escherichia coli*, staphylococci, *Proteus* species, *Veillonella, Fusiformis*, " proteolytes " and fungi are used and references to these in the literature are given; several of them are not well known in Britain.

Among the general conclusions of interest are:—the usual predominance of the lactic acid bacilli, streptococci and acidophilic forms at all sites if both aerobic and anaerobic cultures are considered; the practical limitation of *E. coli* and enterococci to the bowel; the absence of staphylococci from the conjunctiva. The conjunctiva is described as yielding growths only on the optimal general medium and these consist of Gram-positive coccal forms.

The relative abundance of proteolytic forms in the vagina notwithstanding the absence of *E. coli* and enterococci, is considered noteworthy. [It is presumed that the term "*Proteolyten*" covers both aerobic and anaerobic forms and that this is discussed in the paper of one of the authors (Haenel, *Ernahrungsforschung*, 1956, v. 1, 615). Neisseriae and corynebacteria are not discussed and it is difficult to assess the significance of the findings without reference to all papers quoted about the special selective media used.]

J. W. McLeod

HAENEL, H. & MÜLLER-BEUTHOW, W. Untersuchungen post mortem über die Besiedlung des menschlichen Darmkanals. [**Post Mortem Investigation of the Bacterial Flora of the Human Bowel**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 172, Nos. 1/2, 93–112, 10 figs. [36 refs.]

The incidence and relative numbers of the groups of bacteria are already discussed [Haenel *et al.*, above]. These have been investigated at various levels in the alimentary tract at post mortem.

The authors are inclined to believe that where bodies are kept at a reasonably low temperature, these findings give a reliable indication of the conditions existing in the body at the time of death.

In a series of charts these findings are indicated and related to *p*H and solid content of the material withdrawn from the alimentary tract at different levels. The data supplied cover 10 separate cases which differ in several respects one from the other.

The normal healthy condition is assumed to be that in which the *p*H is low in the upper part of the tract and there is an associated absence or marked scarcity of bacterial forms, only proteolytic forms (presumably sporing micro-organisms) being present. Whereas in the colon the bacteriology is very much that of the faeces with lactobacilli, especially anaerobic forms, "bifidus" predominate but enterococci, *Escherichia coli* and proteolytic forms are abundant. The less healthy condition is considered to be that in which there is a higher *p*H in the upper digestive tract associated with staphylococci, fungi and the bacteria of the faeces in varying degrees. *Proteus* was recognized in some part of the intestinal tract in all individuals examined although never in larger numbers.

The authors were unable to relate the presence of paracolon forms to derangement of the intestinal tract and they reject the suggestion that the bacteria in the bowel are there in a condition of symbiosis, *i.e.*, one in which the host and the saphrophyte both enjoy benefits from the association. They consider the presence of bacteria in the tract to be rather an inevitable evil associated with the necessity of controlled defaecation at considerable intervals of time. They argue that, for example, beriberi could not occur if the faecal bacteria were a notable source of elements of the vitamin B group. *J. W. McLeod*

RICHARDSON, R. L. & JONES, Marion. **A Bacteriologic Census of Human Saliva.** *J. Dental Res.* 1958, Aug., v. 37, No. 4, 697–709, 1 fig. [20 refs.]

Each of 14 subjects contributed a specimen of saliva on 10 separate occasions, the 10 separate specimens for any 1 person being collected over a 5-month period. 10 males and 4 females ranging between 25 and 40 years of age were examined. By technical methods, fully given in the paper, attempts were made to enumerate the following in the saliva:—total aerobes and total anaerobes; total streptococci; *Streptococcus salivarius,* neisserias; veillonellas; lactobacilli; fusobacteria; leptotrichias; candidas; salt-tolerant micrococci; starch hydrolysers; coliforms; and hydrogen-sulphide-producing organisms.

The veillonellas, total anaerobes, and total aerobes showed the least fluctuation. There were no statistically significant differences between vegetarians and non-vegetarians. Females had lower counts than males. Population counts of salt-tolerant micrococci, neisserias, leptotrichias, fusobacteria, and hydrogen-sulphide producers provided an index of gingival health. Subjects with high counts in one or more of these categories had varying degrees of gingivitis and calculus deposits.
J. W. Howie

OSTROM, C. A., WOLOCHOW, H. & JAMES, H. A. **Studies on the Experimental Epidemiology of Respiratory Disease. IX. Recovery of Airborne Bacteria from the Oral Cavity of Humans: the Effect of Dosage on Recovery.** *J. Infect. Dis.* 1958, May–June, v. 102, No. 3, 251–7, 2 figs. [22 refs.]

A number of subjects were allowed to inhale, through either a mouthpiece or a facepiece, a cloud of *Serratia marcescens* [*Chromobacterium prodigiosum*], having 90% of its particles 3μ in diameter or less. Immediately after exposure the mouth was sampled by 4 methods: swabbing of the posterior pharynx or of the dorsum of the tongue, or by mouth or "naso-pharyngeal" wash. The mouth wash proved the most efficient. No difference was found between mouth and nasal inhalation, indicating that most of the particles must have penetrated the nasal cavity. From most individuals no more than about 0·1% of the inhaled dose could be recovered. *R. E. O. Williams*

PALVA, T., GRÖNROOS, J. A. & ELO, R. **Cytology and Bacteriology of Bronchial Aspirates.** *Acta Tuberculosea Scandinavica.* 1958, v. 35, Nos. 3/4, 204–216.

ORTALI, V. **A Rapid and Reliable Method for Blood Culture.** *Lab. Practice.* London. 1958, Oct., v. 7, No. 10, 581–3, 2 figs.

The Castenada method was used, but large Roux flasks containing 250 or 1,000 ml. were employed with a strip of agar previously solidified before addition of the broth. When testing the blood of patients under antibiotic treatment, a 1,000 ml. bottle was used and 10·0 ml. of blood in 300 ml. of broth was added. There is no need to use penicillinase or *p*-aminobenzoic acid; the mere dilution of the blood is sufficient to assure a positive culture without regard to the antibiotic used.

Inoculation of the sediment of 10 ml. of centrifuged citrated blood, or of a similar quantity allowed to stand for 2 hours, may yield positive results when whole blood is negative. After inoculation the flasks are incubated at 37°C. and inspected every 24 hours. Afterwards the broth of the negative flasks is allowed to run over the surface of the agar. The time taken for growth ranged from 1 to 5 days, and the average time was 3. Tables show the results for species of *Salmonella, Brucella, Staphylococcus, Streptococcus* and *B. anthracis.*. *P. A. Clearkin*

HARADA, K. **Gram Differentiation without the Use of Iodine.** *Stain Technology.* 1958, Sept., v. 33, No. 5, 205–8. [10 refs.]

The author, from Tokyo, set out to discover to what extent iodine is essential for Gram differentiation. He used *Escherichia coli, Salmonella cholerae suis, Shigella dysenteriae, Proteus vulgaris, Staphylococcus aureus, Bacillus subtilis* and bread yeasts as test organisms and applied as decolorizing agents methanol, ethanol, *n*-butanol, *t*-butanol, *n*-propanol, *i*-propanol, dioxane, acetone and aniline. The stain used was crystal violet (Merck, No. 08212) 0·1% in distilled water and the mordant consisted of 2 gm. iodine and 3 gm. potassium iodide in 300 ml. of distilled water.

The procedures were carried out without the use of

iodine and controlled by the use of iodine as in the usual Gram procedure.

The bacteria in distilled water were smeared on slides dried in air and fixed in a flame. Crystal violet solution was allowed to act for 3 minutes and the slide was rinsed in tap water. Then the slide was either (a) immersed in the iodine mordant for 1 minute and rinsed, or (b) blotted dry. In both cases the smear was then differentiated for 1 minute to 24 hours in the various decolorizers and blotted dry.

The results are shown in a table. Without the use of iodine, methanol was a stronger decolorizer than ethanol and both were stronger than propanol and butanol. Dioxane was weak. Thus, decolorizing power tended to decrease with increasing molecular weight. Acetone and aniline were intermediate in decolorizing power. In every case the order of decolorizing was, Gram-negative cells, *B. subtilis*, *Staph. aureus* and yeasts. When the weaker agents were applied for a moderate length of time, differentiation was possible: this was not possible with methanol and ethanol as all cells lost the dye in a short time. However, the dye was lost with any of the decolorizers if they were used for a long enough time.

With iodine, a longer decolorization time was required in every case than when it was omitted. The iodine seems to be more than an oxidizing agent and must form a dye-iodine complex in the cell. The relative solubilities of this complex in the two types of cells may be regarded as a factor influencing Gram differentiation. In practice methanol, ethanol and acetone gave differentiation in a short decolorizing time, but the other agents required a relatively long time. Some of them produced stippled cells in groups of otherwise strongly Gram-positive cells.

The author concludes that Gram differentiation without iodine may be achieved as follows: stain for 3 minutes or more in 0·1% aqueous crystal violet. Rinse in tap water and blot. Immerse in high molecular weight alcohol, acetone or aniline for 10–60 minutes. Blot.

The mechanism of Gram staining is discussed. Chemical or physical theories or a combination of both have been put forward. The stain has also been explained on the basis of cell wall permeability [see, for example, this *Bulletin*, 1956, v. 31, 64]. The present author postulates that the basic dye penetrates the entire cell and then the decolorizer penetrates it. The dye in the Gram-positive cells is more difficult to remove.

Since iodine penetrates the cell and forms a dye-iodine precipitate and all cells are less permeable for the dye-iodine towards decolorizing agents, slower removal of it results. Gram-positive cells are less permeable to this complex than Gram-negative cells. Strong decolorizers are therefore suitable for regular differentiation when iodine is used, but weak agents are not.

It is therefore concluded that if a high molecular weight alcohol, acetone or aniline is used, iodine is not essential for Gram differentiation. "The normal Gram stain is a property of the entire cell and the cell wall permeability theory fails to explain the presence of stippled Gram-positive cells seen after prolonged differentiation in slow decolorizers."

H. J. O'D. Burke-Gaffney

LINZ, R. & LECOCQ, E. Le sort des bactéries introduites dans la cavité péritonéale du cobaye. [**The Fate of Bacteria introduced into the Peritoneal Cavity of the Guineapig**] *C.R. Soc. Biol.* 1958, v. 152, No. 4, 679–83.

When non-virulent organisms are introduced into the peritoneal cavity of a guineapig which has been prepared by a previous injection of sterile broth, their number decreases rapidly. Virulent organisms, on the other hand, multiply if the dose administered is sufficient to kill the animal, but if the dose is insufficient their number diminishes in the same way as non-virulent organisms. Peritoneal fluid *in vitro* is a favourable medium for the growth of both virulent and non-virulent organisms. The work was done with *Staphylococcus albus, Staph. aureus, Klebsiella pneumoniae* and *Salmonella typhi-murium*.

Charles Wilcocks

PAYNE, J. M. **Changes in the Rat Placenta and Foetus Following Experimental Infection with Various Species of Bacteria.** *J. Path. & Bact.* 1958, Apr., v. 75, No. 2, 367–85, 23 figs. on 8 pls. [17 refs.]

GOLDBERG, L. J., WATKINS, H. M. S., BOERKE, E. E. & CHATIGNY, M. A. **The Use of a Rotating Drum for the Study of Aerosols over Extended Periods of Time.** *Amer. J. Hyg.* 1958, July, v. 68, No. 1, 85–93, 8 figs.

The "Dynamic Aerosol Toroid" is a drum 6 ft. in diameter and 2 ft. wide, which can be rotated in the vertical plane, at 2–3 r.p.m. In it bacterial aerosols with particle diameters of 6μ or less have been kept suspended for up to 2 days, which is 10 times as long as would be possible in a stationary chamber. The apparatus has been used to study the death rate of various bacteria in small particles, and several representative curves are presented. *R. E. O. Williams*

SCHWABACHER, Herta, SALSBURY, A. J. & FINCHAM, W. J. **Blankets and Infection: Wool, Terylene, or Cotton?** *Lancet.* 1958, Oct. 4, 709–12, 5 figs.

During a 4-month period 2 adjacent wards were compared for their air bacterial count by using exposed culture plates. Both wards were equipped with woollen blankets. In 1 the blankets were washed when an infected patient was discharged and otherwise at the Sister's discretion; in the other the blankets were washed after each patient's discharge. The ward with the regularly washed blankets had rather lower total bacterial and staphylococcal counts, with virtual elimination of type-80 staphylococci, which remained present in the control ward.

A second experiment was carried out in a 3-bedded ward in which freshly-washed wool, Terylene or cotton blankets were given to each patient on admission in rotation for periods of 3–5 weeks for each type. The

total and staphylococcal counts were lowest when the cotton blankets were in use; with Terylene the counts were lower than with wool but higher than with cotton. *R. E. O. Williams*

PRESSLEY, T. A. **The Fibre Composition of Hospital Dust.** *Lancet.* 1958, Oct. 4, 712–13, 1 fig. [18 refs.]

Samples of air-borne dust were collected in the wards of 3 hospitals and examined microscopically after staining with the following dye mixture:—Solar Scarlet RL, 3 gm.; Artisil Direct Yellow RGFL ultra dispersed, 3 gm.; Brilliant Alizarine Milling Blue RWL, 5 gm. (all Sandoz); hydrated sodium sulphate 10 gm.; concentrated sulphuric acid 10 ml.; water to 1 litre. Cellulose fibres (for instance, from sheets, towels, etc.) stained pink, protein (largely wool) blue, and nylon green. About 96% of the air-borne fibres proved to be cellulose, and 3·2% protein, and there was no difference between a hospital using all-wool blankets and 2 using wool-cotton mixtures. Most samples examined contained coagulase-positive *Staph. aureus.* It is concluded that wool-blanket fluff is unlikely to be responsible for the air-borne transfer of bacteria. *R. E. O. Williams*

BATE, J. G. & JAMES, Ursula. *Salmonella typhimurium* **Infection Dust-Borne in a Children's Ward.** *Lancet.* 1958, Oct. 4, 713–15.

Over the period December 26, 1956, to November 17, 1957, 21 infants in 1 ward developed infection with *Salmonella typhi-murium*, phage type 2. There were altogether 7 different episodes of infection, the ward being emptied, cleaned and fumigated after each. Yet babies newly admitted to the ward became infected within a few days or weeks. Repeated examinations failed to reveal significant carriers among the staff. The milk feeds were all prepared in a central kitchen which supplied other wards unaffected by the outbreak. A reservoir of infection was eventually found in the dust bag of a floor polisher and it is postulated that this might have been the source of many of the infections. The machine was subsequently fitted with a disposable paper bag. *R. E. O. Williams*

RANGER, I. & O'GRADY, F. **Dissemination of Micro-Organisms by a Surgical Pump.** *Lancet.* 1958, Aug. 9, 299–300, 3 figs.

A suction pump used for drainage of a subphrenic abscess in a ward patient was found to discharge, with the effluent air, large numbers of staphylococci from the pus. Discharge occurred especially at the moment when suction ceased. The air-borne discharge could be prevented by fitting a cotton-wool filter over the outlet of the pump. *R. E. O. Williams*

MACPHERSON, C. R. **Oxygen Therapy—an Unsuspected Source of Hospital Infections?** *J. Amer. Med. Ass.* 1958, June 28, v. 167, No. 9, 1083–6, 1 fig.

Examination of the humidifiers in oxygen apparatus in the wards of a hospital in Columbus, Ohio, revealed that water in the reservoir was very frequently highly contaminated, with coliform organisms, bacilli and *Staphylococcus aureus.* This was not surprising, since the water was often not replaced for long periods, and the apparatus itself could only be disinfected with difficulty. Somewhat stricter rules were therefore adopted. These had, however, only a slight effect on the level of contamination found.

A systematic procedure was therefore adopted in which, among other things, it is laid down that the apparatus must not be used for longer than 1 week without cleaning and sterilization. *R. E. O. Williams*

BACTERIOSTATIC AND BACTERICIDAL SUBSTANCES; DISINFECTION

In this section the abstracts are arranged as far as possible in the following order: General; Antibiotics; Other Therapeutic Substances; Disinfection.

PROC. ROY. SOC. MED. 1958, Oct., v. 51, No. 10, 807–13 (Sect. Epidem. & Preventive Med. 21–7), 5 figs. [16 refs.] **Symposium on Epidemiological Risks of Antibiotics** [LOWBURY, E. J. L.; SELKON, J. B.; SMITH, H. W.].

This report consists of 3 papers.

E. J. L. Lowbury (p. 807) spoke on "Hospital Infection". He contrasts the steadily falling death rate from infective diseases and the falling incidence of some, such as erysipelas, with the continued—and some say increasing—prevalence of hospital infections due to staphylococci and coliform bacilli. He describes his own experience in the burns unit of the Birmingham Accident Hospital, where antibiotics are used to prevent infection by *Streptococcus pyogenes* and *Staphylococcus aureus.* Streptococci have acquired resistance to tetracycline, and staphylococci also to tetracycline and to a much greater degree to erythromycin and to novobiocin when these were used singly: even when the two last-named were used together 20% of doubly resistant strains appeared after 3 months [this *Bulletin,* 1958, v. 33, 205]. Alternative policies are to use antibiotics in rotation or to rely on either antibiotics or synthetic antibacterial compounds to which bacterial resistance does not develop, but "the most profitable line of attack is, undoubtedly, to improve aseptic discipline".

J. B. Selkon (p. 810), discussing "Tubercle Bacilli in the Community", gives information about the frequency of resistance to streptomycin and other drugs based on a survey of 1,344 newly diagnosed and untreated patients in 1955–6 [*ibid.,* 1957, v. 32, 995, *bis*]. The overall frequency of resistance was 5·1%, and for strains from Manchester, Liverpool and Scotland it was higher. It was also higher in young females. In all patients with resistant strains contact with other treated patients was found to have occurred more often than in a matched series of patients infected with sensitive bacilli.

H. W. Smith (p. 812) spoke on "Drug-resistant Bacteria in Domestic Animals". The treatment of mastitis with penicillin, although remaining effective for *Str. agalactiae*, has led to the appearance of resistant strains of staphylococci. The treatment of white scours with streptomycin and other drugs produces resistance to them in *Escherichia coli*: this organism also becomes resistant to tetracyclines in the faeces of pigs and poultry receiving these antibiotics as a feed supplement to promote growth. *L. P. Garrod*

Váczi, L., Barsy, G. & Kubinyi, M. **Changes in the Antibiotic Sensitivity of Pathogenic Bacteria in the Period 1953–1956.** *Acta Microbiologica.* Budapest. 1958, v. 5, No. 2, 151–64. [15 refs.]

This paper is concerned with 8,908 strains of 9 varieties of pathogenic bacteria isolated from 6,765 specimens of material of 7 different kinds (urine, pus, bile, etc.) in the State Institute of Hygiene, Budapest. Particulars are given of the frequency with which each organism was found in each type of material, and the frequency of their occurrence in each of 4 years: the only remarkable feature here is that *Klebsiella* spp. were found in no specimens in 1953, but in 45, 147 and 163, respectively, in 1954, 1955 and 1956. The results of sensitivity tests to penicillin, streptomycin and chloramphenicol are also tabulated, and the percentages sensitive, moderately sensitive or resistant of the principal organisms are given for each of 4 years: tests with oxytetracycline were done only in 1956. The noteworthy changes shown are increases in the frequency of resistance of staphylococci to penicillin (44–71%), of pneumococci to streptomycin (8–49%), of *Escherichia coli* to chloramphenicol (5–26%) and of *Pseudomonas pyocyanea* to chloramphenicol (21–50%). The latter part of the paper deals with correlations between resistance to different antibiotics, and concludes that there are such relationships, although, as the authors admit, the plain facts of their results do not seem to support this. [Nothing is said about how sensitivity tests were done, or at what levels the criteria of resistance were set. Identifying characters are not specified: since 10% of "streptococci" (other than enterococci) were penicillin-resistant, presumably not all were *Streptococcus pyogenes* of Group A. It is also surprising that 5% of pneumococci should be penicillin-resistant. Nevertheless the general trends indicated by the findings are of interest.] *L. P. Garrod*

Boyer, F. Comparaison de l'activité de divers antibiotiques au cours d'infections expérimentales du rat et de la souris. [**Comparison of Activity of Different Antibiotics in Experimental Infection of Rats and Mice**] *Ann. Inst. Pasteur.* 1958, Oct., v. 95, No. 4, 456–62, 5 graphs.

Mice were inoculated intraperitoneally with 0·5 ml. of a 10^{-5} dilution and rats with 1 ml. of a 10^{-3} dilution of culture of *Streptococcus pyogenes, Streptococcus pneumoniae* or *Klebsiella pneumoniae*, and treated with the *same* dose (in each species) of a sulphonamide, a sulphone (DDS), penicillin, streptomycin or chloramphenicol. All untreated controls died. The rats responded much better than the mice to treatment with the 2 synthetic drugs, the larger of the 2 doses used, administered at the time of inoculation and again 1 day later, often saving all the animals, whereas survivors among mice varied from 40% to nil. This difference is attributed to the greater natural resistance of the rat, which enables it to gain more advantage from a purely bacteriostatic drug. On the other hand, treatment with each of the 3 antibiotics was more effective in mice than in rats. [The graphs referred to in the text representing mortality after antibiotic treatment are missing.] *L. P. Garrod*

Hugo, W. B. **Penicillin-Induced Round Bodies in Gram-Negative Bacteria.** [Correspondence.] *J. Pharmacy & Pharmacol.* London. 1958, Sept., v. 10, No. 9, 590–91.

The formation of "round bodies" (sometimes referred to as protoplasts) from *Escherichia coli* and *Salmonella typhi-murium* under the influence of penicillin has been reported. Using similar conditions, the author of this letter has observed the same change in 2 strains of *E. coli*, in *Cloaca cloacae, Citrobacter freundii, Klebsiella aerogenes, Chromobacterium prodigiosum* and 2 species each of *Proteus, Pseudomonas* and *Vibrio*. The concentrations of penicillin required to produce the change (from 25 to 5,000 units/ml.) and the diameter of the bodies formed (mostly 4–6 μ) are stated in a table. *L. P. Garrod*

Eisenberg, G. M., Weiss, W. & Flippin, H. F. **The Influence of Penicillin Therapy on the Emergence of Klebsiellae in Sputum.** *Ann. Intern. Med.* 1958, Aug., v. 49, No. 2, 310–20. [19 refs.]

Penicillin treatment may be followed by the appearance of coliform bacilli in the sputum [this *Bulletin*, 1957, v. 32, 798], and it is commonly believed that these organisms exist in the air passages in small numbers, being enabled to multiply unduly only when much of the remaining flora has been suppressed. These authors have studied the occurrence of the higher serotypes of *Klebsiella* in sputum (the reader being referred to another paper for the criteria by which they were identified) and contest this view about the origins of infections due to them; they suggest that cross-infection from other persons in the hospital environment is more likely to be responsible. 2 experiments were made. In the first, 14 patients were given intramuscular injections of 300,000 units of procaine penicillin twice daily, and their sputum was examined before and after 3 days' treatment in 9 cases, and after 2, 4, 5 and 6 days in the remainder. No *Klebsiella* were recovered from any of them [both dosage and duration of treatment seem inadequate for a test of this kind, and this view is supported by failure to eliminate pneumococci from the sputum of any of 10 patients from whom they were cultivated before treatment]. Secondly 104 specimens from 73 patients were cultivated on a medium containing 5 units of penicillin per ml. as well as on normal medium; there was no significant difference in the frequency with which *Klebsiella* were found on the 2 media. *L. P. Garrod*

KAIPAINEN, W. J. & WIDHOLM, O. **Toxicity of Penicillin to Guinea Pigs.** *Ann. Med. Exper. et Biol. Fenniae.* Helsinki. 1958, v. 36, No. 2, 200–206, 1 fig. [14 refs.]

An explanation suggested for the exceptional toxicity of penicillin in guineapigs is that it causes an overgrowth in the bowel of coliform bacilli, the toxins of which are responsible for the effect [this *Bulletin*, 1956, v. 31, 320]. These authors tried to immunize guineapigs to prevent such an effect: they used the supernatant of a 4-hour glucose peptone water culture of a strongly haemolytic strain of *Escherichia coli*, of which doses were injected intraperitoneally twice or thrice a week for 3 months. The resulting rise in anti-haemolysin titre was small—less than one of the authors had previously obtained in rabbits [*ibid.*, 1953, v. 28, 858]. The effect of 100,000 units of penicillin on these animals was to kill 6 out of 10: the mortality in non-immunized controls was 4 out of 10. [As the authors admit, the toxin they have studied may not be the one that matters in this connexion.] *L. P. Garrod*

MCFARLAND, R. B. **Reactions to Benzathine Penicillin.** *New England J. of Med.* 1958, July 10, v. 259, No. 2, 62–5.

Injections of benzathine penicillin are widely used in the United States armed forces to terminate or prevent streptococcal epidemics. The subjects of the present study were recruits at the Naval Training Center, Bainbridge, Maryland, each of whom "was given an injection of benzathine penicillin G shortly after receiving his other routine inoculations during the winter and spring of 1956–57". Each man was first questioned by a hospital corpsman and then if necessary by the author about previous reactions; 1·8% were "excused" as a result of this. Of 12,858 men given a single dose of either 600,000 or 1,200,000 units, 175 (1·3%) had reactions, all of urticarial or serum sickness type, developing usually 8–15 days later, with a strong tendency to persist or recur. An anti-histamine was of some benefit; in 14 cases the reaction was judged severe enough to require cortisone treatment. The author appears well satisfied that reactions should be so infrequent. [Without denying the possible benefits of this proceeding, particularly for terminating an epidemic rather than preventing one which may never occur, it seems necessary also to recognize that such treatment may itself raise the frequency of sensitivity to penicillin in the treated group.] *L. P. Garrod*

HSU, Irene & EVANS, J. M. **Untoward Reactions to Benzathine Penicillin G in a Study of Rheumatic-Fever Prophylaxis in Adults.** *New England J. of Med.* 1958, Sept. 18, v. 259, No. 12, 581–3. [15 refs.]

The American Heart Association has repeatedly recommended continuous penicillin prophylaxis of rheumatic fever in predisposed subjects regardless of age. Accordingly 32 patients with rheumatic heart disease whose ages varied from 20 to 54 years were given 1,200,000 units of benzathine penicillin intramuscularly at intervals of 1 month for a period in some cases exceeding 2 years and averaging 14·6 months. In 6 of them, all of whom had been given penicillin before, reactions occurred. In 2 these were of serum sickness type, occurring after the first and second injections; in 3 they are described as a pruritic eruption, after the 4th and 10th injection and after a dose of "aqueous" penicillin at an interval after 12 injections, and in 1, a woman aged 54, death from what was regarded as anaphylactic shock occurred a few minutes after the 20th injection. "It is apparent that the parenteral use of penicillin in rheumatic-fever prophylaxis in adults must be carefully weighed against the possible hazards." *L. P. Garrod*

YEH, Fang. **Peripheral Gangrene and Hemorrhagic Purpura due to Penicillin Sensitivity. Report of a Fatal Case.** *Chinese Med. J.* Peking. 1958, June, v. 76, No. 6, 599–601.

A man aged 36, complaining of mild fever accompanied by general discomfort, was given 100,000 units of penicillin intramuscularly. 2 days later erythematous swellings accompanied by pruritus appeared over the trunk and limbs. When he was admitted to the author's hospital, 7 days after the injection, gangrene of the fingers and toes was developing. The original swellings subsided but the peripheral gangrene progressed, fever mounted, purpura developed, and death followed 4 days after admission. No post-mortem is described, and there is no discussion of what the original illness might have been, but reasons are given for regarding the gangrene and purpura as manifestations of penicillin sensitivity. *L. P. Garrod*

ZIMMERMAN, M. C. **Penicillinase-Proved Allergy to Penicillin in Poliomyelitis Vaccine.** *J. Amer. Med. Ass.* 1958, Aug. 9, v. 167, No. 15, 1807–9.

The culture medium used in the production of poliomyelitis vaccine contains 200 units of penicillin and 200 μgm. of streptomycin per ml. The author of this paper has inquired of different manufacturers how much of the penicillin remains in the final product; only 1 make is said to contain a negligible amount. He describes 6 cases in which an injection of the vaccine was followed by a skin reaction, usually of urticarial type, after an interval varying from 1 to 21 days. A history of previous reactions to penicillin was elicited in 5 of these cases. Penicillinase cleared the condition; in 1 case a further dose of the incriminated vaccine was given under penicillinase cover and in others a second dose of the penicillin-free vaccine was given, without ill effects. *L. P. Garrod*

BECKER, R. M. **A New Concept in the Treatment of Penicillin Reactions: Use of Penicillinase.** *Ann. Intern. Med.* 1958, June, v. 48, No. 6, 1228–42.

This author has previously shown that a single injection of penicillinase (a commercial preparation from

Bacillus cereus) will destroy circulating penicillin for several days even during continued treatment with the antibiotic [this *Bulletin*, 1956, v. 31, 1034]. This paper gives 46 case histories, most of them furnished by other practitioners in various parts of the United States, illustrating the effects of penicillinase treatment in patients exhibiting reactions of sensitivity to penicillin. Various forms of penicillin caused these, often procaine or benzathine penicillin, and usually in substantial dose(s), but 1 reaction was attributed to the penicillin content (alleged to be 400 units but unlikely to have been so much) in a dose of poliomyelitis vaccine. The interval between dose and onset of reaction, when stated, varied from 1 hour to 1 month, but seems most often to have been about 10 days; all reactions were urticarial in type, with variations such as involvement of the larynx, vesiculation and exfoliation. In 24 patients, only penicillinase was used in treatment, with uniformly good results; in the remainder antihistamines, steroids, etc., were also given. Only 2 of these cases responded poorly, and in them penicillinase treatment had been long delayed. Many of the patients appear to have needed only 1 dose, usually of about 1,000,000 units. *L. P. Garrod*

Zwart Voorspuij, A. J. & Bokma, L. H. L'action simultanée de deux ou plusieurs substances antimicrobiennes. L'action antibactérienne de la combinaison pénicilline-streptomycine-chloramphénicol sur *Haemophilus influenzae in vitro*. [**Simultaneous Activity of Two or Several Anti-Microbial Substances. Antibacterial Activity of the Penicillin-Streptomycin-Chloramphenicol Combination on** *H. influenzae in vitro*] *Ann. Inst. Pasteur*. 1958, Oct., v. 95, No. 4, 404–12, 5 figs.

Penicillin, streptomycin and chloramphenicol were added alone and in 41 different relative proportions to a fluid medium containing X and V factors, of which further dilutions were made: these were inoculated with a strain of *Haemophilus influenzae* of type B and read for presence of visible growth after 18 hours. These tests were made 15 times and mean values calculated; these are given in a table in terms of μgm./ml. to 3 decimal places. An "index of activity" is then calculated on the basis of deviations from this mean; no details of the latter are given. The activity of mixtures of different proportions of penicillin + chloramphenicol and of streptomycin + chloramphenicol are presented in simple graphs: that of the triple mixture in 3 different complex graphs of triangular shape, some features in which are said to indicate antagonism. The authors propose this method of studying and analysing the results of combined action, but draw no practical conclusions from their findings. *L. P. Garrod*

Katayama, T. **Studies on the Interaction of Streptomycin with Acidic High Polymers of the Tubercle Bacilli.** *Nagoya J. Med. Sci.* 1958, Sept., v. 21, No. 3, 165–80, 20 figs. [35 refs.]

Bowman, Frances W. & Holdowsky, S. **Survival of Bacteria in Dihydrostreptomycin Solutions for Injection.** *Antibiotics & Chemotherapy*. New York. 1958, Aug., v. 8, No. 8, 406–9.

The official method for testing dihydrostreptomycin for sterility is to cultivate 0·5 gm. in 75 ml. of medium; naturally this will not detect the presence of sensitive or moderately resistant contaminants. The authors (who work in the Department of Health, Food and Drug Administration, Washington) compared this with the membrane filter method [this *Bulletin*, 1957, v. 32, 604], in which the antibiotic can be washed away, applying the 2 tests to solutions of the antibiotic made in suspensions of 20 species of bacteria of different strengths and kept at room temperature for 1, 2, 4 or 7 days or longer. Sensitive vegetative organisms were not recovered in culture by either method (they were apparently killed within 1 day). Highly resistant vegetative organisms were recovered by either method (except a streptomycin-dependent strain, which naturally only grew in a culture made by the official method). Sensitive sporogenous organisms of 6 species were recovered only by the membrane filter method. Despite this proved advantage of the latter, the authors consider that the amount of manipulation involved in it, which can lead to extraneous contamination, contra-indicates its adoption in its present form. *L. P. Garrod*

Rubin, D., Weisberger, A. S., Botti, R. E. & Storaasli, J. P. **Changes in Iron Metabolism in Early Chloramphenicol Toxicity.** *J. Clin. Investigation*. 1958, Sept., v. 37, No. 9, 1286–92, 4 figs. [16 refs.]

These authors have studied "abnormalities of ferrokinetics" in patients treated with chloramphenicol. They were given an intravenous injection of 10 μc. ^{59}Fe (as ferrous citrate) added to plasma. Of 15 patients, 10, given 0·75–3 gm. chloramphenicol daily for periods varying from 3 to 34 days, handled this iron normally, while in 5, given 1–4 gm. daily for 7–21 days (some of whom were included "because of apparent haemopoietic changes"), the radio-active iron disappeared abnormally slowly from the blood, and subsequently failed to appear in circulating erythrocytes for 8 or more days; it was also observed that radio-activity was greater in the liver than in the bone marrow and that a rise occurred in the plasma iron and the percentage saturation of the plasma iron-binding globulin. Thus these patients had a temporary arrest of red cell formation; in 1 the formation of leucocytes and platelets was also affected. In 2 patients these tests were carried out with the results described before anaemia had developed. "Determination of the plasma iron pattern" is suggested as a means of early detection of toxic effects during chloramphenicol administration. *L. P. Garrod*

Kunin, C. M., Jones, W. F., Jr. & Finland, M., with the technical assistance of Clare Wilcox & Ann Najarian. **Enhancement of Tetracycline Blood Levels.** *New England J. of Med.* 1958, July 24, v. 259, No. 4, 147–56, 5 figs. [19 refs.]

This paper describes 3 separate studies of the absorption of tetracycline in different forms, carried out by the cross-over method, in which a dose of each preparation is administered to each normal subject at different times and blood levels are determined at intervals. The first experiment, carried out late in 1956, compared tetracycline hydrochloride with tetracycline phosphate complex; the second, in 1957, compared these 2 preparations and tetracycline base with sodium hexametaphosphate or monobasic sodium phosphate. The differences observed were not statistically significant, and the comparison is invalidated by the presence in some of the capsules of calcium phosphate as a filler.

In the final experiment, carried out in 1958, this factor was eliminated, and 4 preparations, 2 of them new, were compared. Blood levels were determined by a tube dilution method in the authors' laboratory, and the same specimens were assayed in 2 manufacturers' laboratories by the cup-plate method. Results were corrected for the actual content of the capsules used, as determined by the Antibiotics Division, Food and Drug Administration, Washington (this varied from 205 to 265 mgm. in a 250 mgm. capsule). The best absorbed preparation was one containing tetracycline hydrochloride and citric acid; then in order of diminishing absorption were tetracycline hydrochloride with glucosamine hydrochloride, tetracycline phosphate complex, and tetracycline hydrochloride alone. The difference between the first and the last of these was statistically significant; others are said not to be.

The authors doubt whether the degree of enhancement of absorption obtained with these newer preparations is "clinically important" [certainly this has not been "proved", but if the enhancement is genuine, why not take advantage of it?]. They also criticize other less carefully controlled recent studies of this nature and protest against the firm conclusions drawn from them. *L. P. Garrod*

ZISCHKA, W. & PROHASKA, E. Über die Ansiedlung von oral applizierter tetracyclinresistenter Escherichia coli im Darm während der Therapie mit Antibiotica der Tetracyclinreihe. [**The Fate of Ingested *E. coli* Resistant to Tetracycline during the Administration of Tetracyclines**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 172, Nos. 5/6, 433–6. [10 refs.]

Normal individuals swallowed 3 times a day for 4 days 20 mgm. of a lyophilized preparation of a highly tetracycline-resistant strain of *Escherichia coli*. Some of them were also given 1 gm. daily of tetracycline, oxytetracycline or Hostacyclin during these 4 days and for up to 10 further days. Stools were cultivated daily on normal medium and on medium containing tetracycline. The resistant strain appeared only very transiently and in small numbers in subjects given no antibiotic; in those given any of the tetracyclines resistant organisms were numerous in the cultures during medication, but disappeared within a few days when it ceased. *L. P. Garrod*

LUTZ, A., WITZ, M. A. & SCHAEFFER, A. Recherches sur l'évolution de la résistance de germes du genre *Proteus* aux antibiotiques usuels de 1950 à 1958. L'action *in vitro* de la novobiocine, de la kanamycine, de la nitrofurantoïne, et des sulfamides. [**Studies on the Evolution of Resistance of the Genus *Proteus* to Routine Antibiotics from 1950 to 1958. *In vitro* Activity of Novobiocin, Kanamycin, Nitrofurantoin and Sulphonamides**] *Ann. Inst. Pasteur.* 1958, Oct., v. 95, No. 4, 413–23. [21 refs.]

These workers in Strasbourg have determined the minimum inhibitory concentration of various antibiotics and synthetic drugs for many strains of 4 species of *Proteus*. Their comparisons between isolations in 1950, 1954–5 and 1957–8, show some diminution in the frequency of resistance to chloramphenicol and to streptomycin and little change in that to tetracycline. They also present findings, unrelated to different periods of isolation, concerning sensitivity to other drugs. Most strains of *Pr. mirabilis* were sensitive to about an equal degree to both penicillin and synnematin B; *Pr. vulgaris*, *Pr. morganii* and *Pr. rettgeri* were resistant to both. The 2 last-mentioned were also frequently highly resistant to novobiocin, the other 2 species being usually sensitive. Full sensitivity to sulphonamides was seen only in *Pr. mirabilis* (6/35 strains), but the species most sensitive to nitrofurantoin was *Pr. morganii*. Strains of all species were fairly uniformly sensitive to both framycetin and kanamycin. *L. P. Garrod*

DAY, H. J., CONRAD, F. G. & MOORE, J. E. **Immunothrombocytopenia induced by Novobiocin.** *Amer. J. Med. Sci.* 1958, Oct., v. 236, No. 4, 475–82, 2 figs. [17 refs.]

"A case history of an immunothrombocytopenia caused by novobiocin is described. Sensitivity to novobiocin was substantiated by reproducing a thrombocytopenia with readministration of this drug. Platelet agglutinins and lysins were demonstrated in the patient's blood plasma and serum. Immunologically adapted clot retraction, prothrombin utilization, and optical clearing tests showed evidence of impaired platelet function. Evidence is presented that the defect is a quantitative one and does *not* interfere qualitatively with thromboplastin generation."

SEIGNEURIN, R., MAGNIN, R. & FILS, J. Courbes de croissance de staphylocoque dans un milieu additionné d'hématies ayant fixé un antibiotique. [**Growth-Curves of a *Staphylococcus* Strain in a Medium containing Erythrocytes which have adsorbed an Antibiotic**] *Ann. Inst. Pasteur.* 1958, July, v. 95, No. 1, 114–17, 1 fig.

Human red cells were suspended in a solution of Magnamycin for 48 hours at 4°C., and were then washed 3 times. Suspensions of staphylococci mixed with the heated red cell suspension, or with the same suspension haemolysed, died as quickly as cocci suspended in a Magnamycin solution of corresponding

strength. The drug must therefore have been adsorbed to the red cells and not eluted by washing, but was nevertheless active. *R. E. O. Williams*

JONES, W. F., Jr. & FINLAND, M., with the technical assistance of Clare WILCOX and Ann NAJARIAN. ***In vitro* Observations on A-8506 (Bryamycin).** *Antibiotics & Chemotherapy.* New York. 1958, Aug., v. 8, No. 8, 387–91, 1 fig.

Bryamycin is an antibiotic isolated from *Streptomyces hawaiiensis* n. sp. by workers of Bristol Laboratories Inc. [this *Bulletin*, 1956, v. 31, 854]. The present authors have determined the minimum inhibitory concentration of this substance for a wide range of bacteria; all Gram-positive cocci were highly sensitive (*Sarcina*, pneumococcus, 3 main species of streptococcus and staphylococci); 101 strains of *Staphylococcus aureus* were tested without finding a naturally resistant strain. All Gram-negative organisms, including even *Haemophilus* and *Neisseria* spp., were much more resistant. Staphylococci were rendered resistant; the process was gradual at first, but a sudden increase to high resistance occurred after about 25 transfers. The sensitivity of these resistant variants to 12 other antibiotics was compared with that of the parent culture; apart from some *diminution* of resistance to 4 of these there was no change. Staphylococci habituated to erythromycin, carbomycin, oleandomycin, spiramycin or streptogramin underwent no significant change in sensitivity to bryamycin. *L. P. Garrod*

PARFENTJEV, I. A. **Yeast Antibiotic with Therapeutic and Prophylactic Properties.** *J. Infect. Dis.* 1958, July–Aug., v. 103, No. 1, 1–5.

This paper from the Department of Microbiology at Yale makes some sensational claims which are likely to be received with considerable reserve, particularly since full protocols of the experiments on which they are based are not given. The antibiotic, to which the name malucidin has been given, is obtained by the alkaline extraction of yeast, and is said to be a protein. It has been found to protect laboratory animals against infection with a variety of Gram-positive and Gram-negative bacteria, and with *Candida albicans*. In one experiment a (? single) dose of 0·024 mgm. saved 10/10 mice inoculated with *Staphylococcus aureus* and 9/10 inoculated with *Pseudomonas pyocyanea*, all controls dying. It can be given by all usual injection routes, and in one experiment it reduced the mortality of mice inoculated with *Proteus vulgaris* intraperitoneally when administered intranasally; promising results have also been obtained from administration per rectum. The unusual choice of *Proteus vulgaris*, injected intraperitoneally in doses of several billion, was made for an experiment to demonstrate the lasting protection conferred by a single dose of malucidin. When inoculation followed this after an interval of 1 month, 25/36 mice survived, all controls dying. The blood of treated animals could not be shown to possess bactericidal properties *in vitro* or the capacity to confer protection on other animals. *L. P. Garrod*

ESSELLER, A. F., HUNZIKER, H. & GOLDSAND, R. Klinische Erfahrungen mit Orisul, einem langwirkenden Sulfonamide. **[Clinical Experiences with Orisul, a Long-Acting Sulphonamide]** *Schweiz. med. Woch.* 1958, Aug. 16, v. 88, No. 33, 813–17, 3 figs. [19 refs.]

This paper is in praise of 3-(*p*-aminobenzenesulphonamido)-2-phenyl-pyrazole (Orisul, Ciba). Pharmacological studies were carried out in 54 subjects, and showed that although absorption is fairly rapid, excretion is slow; only up to 11% of the drug in the blood is acetylated, and 27% in the urine. The findings indicated that a single daily dose should maintain an adequate blood level, and the dose usually given in a therapeutic study in 120 patients was 1·5 gm.; this was given twice daily in severe cases, and a few patients were given injections of the sodium salt, 0·5 gm. or 1 gm. twice daily (said to be administrable either intravenously or intramuscularly, and having a *p*H of 9). Most of these patients had infections of the urinary tract or lungs, the latter including several forms of pneumonia, and the majority of them responded well to the treatment. A table of bacteriological findings, unrelated to diagnoses, is given; only 8 organisms of 5 species were found to be sulphonamide-sensitive, and in 6 of these cases treatment succeeded; 55 of 9 species were resistant but treatment nevertheless succeeded in 36 of the patients from whom they were derived.

The somewhat optimistic tone of the paper is also illustrated by the record of uniform success in the treatment of chronic cholecystitis, chronic cholangitis, diverticulitis and furunculosis (1, 2, 2 and 2 cases, respectively). The drug was well tolerated, with few and unimportant side-effects; one of the authors took 25 gm. daily for 5 days and was none the worse!

L. P. Garrod

GOLDHAMMER, H. Das Sulfonamid 3-(p-Aminobenzol-sulfonamido)-2-phenyl-pyrazol. Pharmakologische und klinische Eigenschaften. **[The Clinical Pharmacology of a New Sulphonamide ("Orisul")]** *Deut. med. Woch.* 1958, Aug. 29, v. 83, No. 35, 1488–94, 1527, 4 figs. [14 refs.]

This paper reports some interesting findings with regard to the behaviour in the body of 3-(*p*-aminobenzenesulphonamido)-2-phenyl-pyrazole (Orisul). Serial estimations in the blood and urine after administering single doses of 1·5 or 3 gm. to patients showed a peak level in the blood of 10–>12 mgm. per 100 ml. at 4 hours falling to about 2–4 mgm. per 100 ml. at 24 hours, with corresponding findings in the urine. In 8 patients 10 series of estimations were carried out in both serum and whole blood, showing that remarkably little of the drug is contained in the red cells: the partition coefficient cell-concentration/plasma-concentration varied from 0·012 to 0·085, whereas that for 4 other sulphonamides is given as varying from 0·31 to 1·6. The concentrations in different organs were also determined in 2 patients who died during treatment: high levels were found in the kidneys, uterus and lungs and the lowest level in heart muscle. Calculation of partition coefficients between organs and blood on the

basis of these findings and comparison with existing data for other sulphonamides show that tissue concentrations for Orisul are exceptionally high. The brain could not be examined in either of these cases, but examinations of cerebrospinal fluid showed the concentration attained in this to be exceptionally low. Information is also given about the degree of acetylation of the drug in the blood, urine and various organs examined; this was generally low. *L. P. Garrod*

BACHMANN, D., PAULY, H. & SCHMIDT, W. Erfahrungsbericht über die klinische Anwendung eines neuen Sulfonamids mit Depot-Charakter. [**Preliminary Clinical Results with a New Sulphonamide ("Orisul"): 3-(p-Aminobenzenesulphonamido)-2-phenyl-pyrazole**] *Deut. med. Woch.* 1958, Aug. 29, v. 83, No. 35, 1494–1500, 5 figs. (1 on pl.)

This paper describes a purely clinical study of sulphaphenazole (Orisul). Some estimations of the drug in the blood showed that satisfactory levels could be maintained by giving 1 gm. at 12-hour intervals to adults. Therapeutic results were good in 23/31 cases of lobar and bronchopneumonia (no bacteriological data) in only 1/12 cases of virus, suppurative or "infarction" pneumonia, in 9/10 cases of tonsillitis, 5/8 urinary infection and in 4 of *Salmonella* enteritis. Similar findings are given for infections in infants and children, among whom 23/27 cases of acute otitis media also responded well: it appears that a single daily dose was found adequate at this age. The drug was well tolerated. *L. P. Garrod*

NEIPP, L., PADOWETZ, W., SACKMANN, W. & TRIPOD, J. Experimentelle Untersuchungen über neue Sulfonamidderivate unter besonderer Berücksichtigung der Beziehungen zwischen Blutkonzentration, Intensität und Dauer der Heilwirkung. [**Experimental Studies of New Sulphonamide Derivatives with particular reference to Relations between Blood Concentration and Degree and Duration of Therapeutic Effect**] *Schweiz. med. Woch.* 1958, Aug. 23 & 30, v. 88, Nos. 34 & 35, 835–9; 858–63, 12 figs. [23 refs.]

This important paper from the Ciba Laboratories describes a searching experimental study of the properties of 6 sulphonamide compounds. These were 3-(*p*-aminobenzenesulphonamido)-6-chlorpyridazine (sulphachlorpyridazine), 3-(*p*-aminobenzenesulphonamido)-2-phenyl-pyrazole (sulphaphenazole), 3-(*p*-aminobenzenesulphonamido)-2-phenyl-5-methyl-pyrazole (sulphamethylphenylpyrazole), sulphamethoxypyridazine, sulphasomidine and sulphisoxazole. The 2 last-named were included only for comparison, and the tests applied make them appear very inferior to their long-acting successors. It is possible to give only a general account of the nature of these experiments and of the main features in the results.

In vitro activity. There were few material differences in the capacity of these compounds to inhibit the growth of 9 species of bacteria *in vitro*: one exception is the greater activity of sulphachlorpyridazine against *Escherichia coli*.

Therapeutic effect in mice. Against haemolytic streptococcal infection in mice the order of activity of the 3 most active compounds was sulphaphenazole, sulphamethylphenylpyrazole, sulphamethoxypyridazine. This order was confirmed in therapeutic tests in which the interval between doses was extended from 1 to 2, 3 and 4 days and in which inoculation followed subcutaneous injection of a suspension of the drug after an interval of up to 10 days.

Blood concentrations. The best sustained blood levels in almost all tests in several animal species were obtained with sulphamethylphenylpyrazole: sulphaphenazole came next in the mouse and the rabbit, but sulphamethoxypyridazine in the dog.

Distribution between cells and plasma. The 2 new Ciba compounds present an extraordinary contrast: sulphamethylphenylpyrazole attains an actually higher concentration in the red cells than in the plasma (probably accounting for its slow excretion), while the cell concentration of sulphaphenazole is only about 20% of that in the whole blood. All other values were intermediate.

Excretion in urine and bile. The rate of urinary excretion corresponded to the findings for persistence in the blood. In bile the highest concentrations were attained by sulphamethylphenylpyrazole and sulphachlorpyridazine [no details are given].

Organ distribution. The compounds were assayed in the liver, kidneys, lung and muscle of mice: most of the levels found did not exceed those in the blood.

Information is also given about degrees of acetylation and toxicity. The 2 main general conclusions reached are that the blood concentrations attained do not alone determine therapeutic effect (*i.e.* there are intrinsic differences in therapeutic activity) and that the possibilities of the sulphonamides have not yet been exhausted. *L. P. Garrod*

PETRIE, E. M. & ROMAN, D. P. **Chlorine Sanitizing Compounds.** *Soap.* New York. 1958, Aug., v. 34, No. 8, 67–8, 99–101.

This paper commends 2 new organic chlorine compounds, di- and trichloroisocyanuric acid, as the active ingredients of "sanitizers". A list of suitable "fillers" is given. Those used in some tests of stability were sodium tripolyphosphate, sodium sulphate and alkyl aryl sulphonate: when a mixture so compounded was kept at 100°F. in 60% relative humidity for 75 days, the percentage of available chlorine fell from 10 only to 7·8. Some experiments are described showing that solutions of sanitizers containing trichloroisocyanuric acid, having a *p*H varying between 8·1 and 10·7, and diluted to contain 50 or 100 p.p.m. of available chlorine, all kill a heavy inoculum of *Escherichia coli* or *Staphylococcus aureus* in 30 seconds. These compounds have a low oral toxicity, and "immersion studies" in human beings gave no evidence of any irritant, sensitizing or "fatiguing" effect. *L. P. Garrod*

McCarthy, B. J. & Hinshelwood, C. **The Action of Two Antibacterial Agents on the Growth of** *Bact. lactis aerogenes. J. Chem. Soc.* 1958, June, 2269–75, 5 figs. [Refs. in footnotes.]

The 2 antibacterial agents studied had quite different effects. When *Bacterium lactis aerogenes* was cultivated in a medium containing disodium dihydrogen ethylenediamine-NNN′N′-tetra-acetate in concentrations varying from 5 to 10,000 mgm./ml., the only effect was a reduction in the rate of growth proportional in degree to concentration: such growth curves therefore have a fan-like distribution. After repeated transfer in a medium containing 10 or 100 mgm./ml. the generation time progressively diminishes, but without returning to normal

The effect of 2:4-dinitrophenol is to prolong the lag period. The organism was trained to withstand concentrations varying from 200 to 3,000 mgm./ml., and the length of the lag period in media containing different concentrations was then shown to vary with the concentration to which it had been trained. These experiments support the idea of a change of adaptive nature affecting most of the population and to an indefinitely variable degree depending on the extent of training, rather than the selection of initially resistant cells. That a high proportion of cells undergoes this change was also shown when trained and untrained cells were plated on dinitrophenol agar: the expected number of colonies of the untrained cells appeared after a delay. Trained organisms showed a diminished capacity to adapt to new sources of carbon. *L. P. Garrod*

Muroma, A. **Studies in the Bactericidal Action of Salts of Certain Rare Earth Metals.** *Ann. Med. Exper. et Biol. Fenniae.* Helsinki. 1958, v. 36, Suppl. 6, 54 pp. [Numerous refs.]

This monograph begins with a review of the literature of its subject, which, as regards some of the metals considered, is scanty. The author's own experiments were made with the chlorides of scandium, yttrium, lanthanum, cerium, praseodymium, neodymium, samarium, europium and ytterbium. Since these are very costly, it was impracticable to carry out tests of bacteriostatic action in which the salts were incorporated in a culture medium; only tests of bactericidal action were made, and in these only small volumes were used. The mixture consisted of 0·9 ml. of decimal dilutions of a solution of the salt + 0·1 ml. of a bacterial suspension, the final molar concentration of the salts ranging from 10^{-1} to 10^{-7}. A loopful of the mixture was cultivated in broth after 5 minutes and 1 and 24 hours. The bacteria were *Staphylococcus aureus, Streptococcus pyogenes, Str. faecalis, Bacillus subtilis, Escherichia coli, Salmonella typhi-murium, Salm. paratyphi B, Salm. typhi, Shigella dysenteriae, Sh. flexneri, Klebsiella pneumoniae, Proteus mirabilis* and *Pseudomonas pyocyanea;* 2 strains of most of these species were tested.

The results are given in full in 13 pages of tables. *B. subtilis* is omitted because it survived in every tube, and 24-hour results for *Salm. typhi* and *Ps. pyocyanea* are also not given because these organisms failed to survive for this time in distilled water. There is little of interest otherwise in the susceptibility of individual species; Gram-negative bacilli were on the whole killed more rapidly than Gram-positive cocci. Most of the salts were bactericidal, at least in 24 hours, in a concentration of 10^{-4}M, some at 10^{-5}M, and one, that of scandium, sometimes at 10^{-6}M. Rate of bactericidal action does not vary, as it has been said to do among other metals, with atomic weight; on the other hand it does in this series correspond with the *radius* of the metallic ion; that of Sc, the most active, is given as 0·83Å and that of lanthanum, one of the least active, as 1·22Å. Since the strength of chelation varies with the radius of the ion, the observed differences in antibacterial activity may depend on capacity to form chelates.

"Paradoxical" findings were common, *i.e.* survival in a concentration higher than another found to be bactericidal. These were abolished by testing in saline or glucose solution [the author does not say whether they were constantly reproducible in tests with distilled water]. One possible explanation is varying degrees of agglutination; different concentrations of lanthanum salts have previously been shown to have such an effect. *L. P. Garrod*

Brumfitt, W., Wardlaw, A. C. & Park, J. T. **Development of Lysozyme-Resistance in** *Micrococcus lysodiekticus* **and its Association with an increased O-Acetyl Content of the Cell Wall.** *Nature.* 1958, June 28, v. 181, 1783–4, 1 fig. [19 refs.]

The first-named author has previously reported that *Micrococcus lysodeikticus* [the name is mis spelt in the title and text of the present paper] can be rendered highly resistant to lysozyme by growth on nutrient agar containing increasing concentrations. It has now been found that the cell walls of the resistant organisms have a greatly increased O-acyl content. A possible explanation appeared to be that in the resistant organism hydroxyl groups which are normally free are acetylated. This was supported by 2 observations; sensitive cell walls could be rendered resistant to lysozyme by acetylation with acetic anhydride and pyridine, and resistant ones could be rendered more sensitive by treatment with alkali. The latter observation was confirmed by mild alkali treatment of intact resistant cells; up to *p*H 11·4 there was progressive reduction in O-acyl content and increase in lysozyme sensitivity, without loss of viability. In a further discussion of the bearing of these observations on the mode of action of lysozyme it is suggested that this action may be to break the linkage between N-acetyl muramic acid and N-acetyl glucosamine; resistant species might then be those not having this bond. *L. P. Garrod*

INDIVIDUAL BACTERIA

In this section the abstracts are arranged as far as possible in the following order: General; Enteric Organisms; Corynebacterium, Mycobacterium; Staphylococcus; Streptococcus; Brucella; Haemophilus; Pasteurella; Pseudomonas; Neisseria; Donovania; Spirochaetes, Leptospira; Anaerobes; Bacillus; Others.

ROBINSON, R. G. **The Isolation of Enteric Organisms from Sewage and the Development of the "Sewage Pad" Technique.** *J. Med. Lab. Technol.* 1958, Apr., v. 15, No. 2, 79–95. [13 refs.]

A modified sewage swab [see MOORE, this *Bulletin*, 1949, v. 24, 187] technique is described. The swab is made of about 2·5 gm. of alginate wool and is about 3 inches square. The edges are stitched with linen thread to prevent disintegration. After immersion in sewage for 48 hours the pad is incubated in 50 ml. selenite F broth, together with 7 ml. of 10% sodium hexametaphosphate to promote solution of the wool, and it is then subcultured on to a solid medium.

When tested in parallel with the gauze swabs it was found that the alginate swabs grew approximately twice as many enteric organisms. The maximum yield of *Salmonella typhi* was obtained after about 6 hours' incubation and of *Salm. paratyphi B* after 18–24 hours. It is recommended that if only 1 subculture is possible it should be after 18 hours' incubation.

J. Nagington

HO, M. & KASS, E. H. **Hemolytic Anemia in Rabbits following Injection of Bacterial Endotoxin.** *Proc. Soc. Exper. Biol. & Med.* 1958, Mar., v. 97, No. 3, 505–9, 2 figs. [17 refs.]

In 3 of 6 normal rabbits given an intravenous injection of *Salmonella typhi* endotoxin a mild haemolytic anaemia occurred 4–15 days later. There was a mild reticulocytosis and the fall in haemoglobin level was of the order of 1–2 gm.% (normal level 10·5–14 gm.%).

A more pronounced anaemia was produced in previously immunized rabbits when they were given a series of daily endotoxin injections. A reticulocytosis occurred after 7–10 days and the maximum observed fall of haemoglobin level was from 12 to 8 gm.%. There was an accelerated rate of erythrocyte destruction which began at about the 8th day. The process was self-limiting and although the daily endotoxin injections were continued the haemoglobin level returned to normal in about 4 weeks.

The increased erythrocyte destruction could not be shown to be due directly to the presence of antibody or to the attachment of endotoxin to the erythrocytes. Their fragility remained unchanged and when injected into normal rabbits they had a normal life. It is presumed that the phenomenon was associated with increased activity of the reticulo-endothelial system.

J. Nagington

SCHMIDT, B. & LENK, V. Ergebnisse der Lysotypie von *Salm. paratyphi B* in Berlin. [**Results of Phage-Typing of** *Salm. paratyphi B* **in Berlin**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1958, July–Aug., v. 116, Nos. 1/2, 15–30, 1 fig. [68 refs.]

Over 2,100 strains of typhoid and paratyphoid B were received for phage-typing in the Institute for Hygiene and Medical Microbiology in Berlin. The results of typing 445 strains of paratyphoid B, isolated from patients in 390 epidemiological foci, are given in this article. They show that the frequency (in percentage of foci) of phage types was as follows: Taunton, 28·7%; type 1, 19%; BAOR, 13·8%; type 3aI, 12·6%; type 3aIvar., 7·9%; type 3a, 6·4%. Phage types 2, Jersey, Beccles and Dundee were infrequent; phage type 3b was not found. In a former communication the finding of the rare phage type 2 in West Berlin was mentioned. This type was not found in Germany or in other Continental countries until 1955, although the percentage found in England varied between 4·3 and 9·9.

A comparison between the phage types in Berlin, West Germany, Middle Germany and England shows that in England type 1 is most common, while in Germany type Taunton is most frequently found. Most striking is the frequency of type BAOR in Berlin.

Phage type 1 was isolated most frequently from waste water in Berlin and type Taunton from chronic carriers.

It is concluded that the type specificity of *Salmonella para-typhi B* phage is not so great as the specificity of Vi phage for *Salm. typhi*. Nevertheless the phage type of paratyphoid B is suitable for epidemiological observations.

P. A. Clearkin

FUKUDA, T., SASAHARA, T., KITAO, T., TANIGAWA, H., FUKUMI, H. & MURATA, Y. **A New** *Salmonella* **Type: Salmonella Miyazaki (9, 12: 1, z13: 1, 7).** *Japanese J. Med. Sci. & Biol.* 1958, Apr., v. 11, Nos. 1/2, 13–14.

"A new microorganism with biochemical reactions typical for the Salmonella group is described, isolated from the feces of the members of a family suffering from acute gastroenteritis. The antigenic formula can be expressed as 9, 12 : 1, z13 : 1, 7. The name *Salmonella miyazaki* is suggested for this culture."

ROHDE, R. & BISCHOFF, J. Ein neuer Salmonellatyp (Salmonella Blankenese) = 1,9,12: b: z_6. [**A New Salmonella Type, Salm. Blankenese, 1,9,12: b: z_6**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 173, Nos. 1/2, 55–8.

WITTIG, H., SULZBACHER, F. & SEELIGER, H. P. R. Ein neuer Salmonella-Typ: S. Halle (mit einem Hinweis auf die Schildkröte als Salmonella-Reservoir). [**A New Salmonella Type, Salm. Halle (with Reference to the Tortoise as a Reservoir**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 173, Nos. 1/2, 159–60.

ERLANDSON, A. L., Jr. & MACKEY, W. H. **Growth and Manometric Studies on Carbohydrate Utilization by** *Shigella flexneri*. *J. Bacteriology*. 1958, May, v. 75, No. 5, 530–34.

Carbohydrate utilization by *Shigella flexneri* was investigated with 18 representative strains and 14 carbohydrates. D-glucose, D-mannose, D-fructose and D-galactose could all function as the sole carbon source for all the strains tested. They were fermented and they stimulated the oxygen uptake of non-proliferating cells.

Trehalose was fermented by all the strains but not all were able to utilize it as the sole carbon source. Those which could do so were also capable of its oxidative dissimilation. This was in general true for sucrose also. None of the other carbohydrates was able to support growth.

It is considered that there is a definite relationship between the ability of non-proliferating cells of *Sh. flexneri* to dissimilate oxidatively certain carbohydrates and the ability of the carbohydrates to support growth as the sole source of carbon in a chemically defined medium. *J. Nagington*

FORMAL, S. B., DAMMIN, G. J., LABREC, E. H. & SCHNEIDER, H. **Experimental Shigella Infections: Characteristics of a Fatal Infection produced in Guinea Pigs.** *J. Bacteriology*. 1958, May, v. 75, No. 5, 604–10, 4 figs.

Fatal infections can be produced in guineapigs by the oral administration of *Shigella flexneri* if they are first deprived of food for 4 days and only provided with water. Then 125 mgm. $CaCO_3$ in 5 ml. distilled water is introduced by means of a stomach tube and the challenge dose of organisms given the same way 3 hours later, followed, after 1 hour, by the intraperitoneal injection of 1·0 ml. of tincture of opium.

Guineapigs which succumbed to a dose of 2×10^7 *Sh. flexneri* 2a died in 24–48 hours and did not have diarrhoea. Animals killed with doses of less than 10^7 organisms died in 72–96 hours and some of these did have diarrhoea. The animals which died had isolated areas of ulceration in the caecum and colon similar to the lesions described in man. In most of the animals which survived the challenge dose it was found that the infecting bacteria were cleared from the alimentary canal within 96 hours. *J. Nagington*

COFFIN, G. S. & SWECKER, E. E. **Two American Strains of** *Shigella flexneri* **resistant to the Common Antibiotics.** *Antibiotic Med.* New York. 1958, Aug., v. 5, No. 8, 533–5.

Of 2 strains of *Sh. flexneri* isolated in Baltimore from children with dysentery, both were resistant to sulphonamides and tetracyclines and 1 also to streptomycin and chloramphenicol. *L. P. Garrod*

BANERJEA, A. **Variations in Protein and Amino-Acid Contents between Smooth and Rough Forms of Certain Serotypes of** *Escherichia coli* **and their relation to DNA Contents.** *Ann. Biochem. & Exper. Med.* Calcutta. 1957, v. 17, No. 6, 199–202. [18 refs.]

The protein and amino acid components of the S (smooth) and R (rough) variants of 4 pathogenic strains of *Escherichia coli* were estimated by a chromatographic method in which hydrolysates of dried bacteria were used.

The R forms of *E. coli* 0111:B4, 055:B5 and 086:B7 contained 5–12% less protein than the S forms. The R variant of 026:B6 differed by containing 3·75% more protein than the S form. In the first 3 there was also a reduction in the DNA content although it did not appear to be quantitatively related to the protein loss. In all the R variants there was less lysine, valine and phenylalanine than in the S forms. Histidine was reduced in all except 086:B7, arginine in all but 055:B5 and tyrosine in all but 026:B6. Ergothioneine was present in all the S forms and was completely absent from the R forms of 0111:B4 and 055:B5. All of the R forms contained an increased amount of aspartic acid. *J. Nagington*

GUPTA, N. P., GUPTA, S. P. & BARUA, D. **Haemagglutination by Strains of** *Escherichia coli* **isolated from Cases of Urinary Infection.** *Indian J. Med. Res.* 1958, Mar., v. 46, No. 2, 147–51. [21 refs.]

164 of 345 strains of *Escherichia coli* from urinary infections agglutinated erythrocytes of one or more animal species. Guineapig erythrocytes were the most frequently agglutinated (71 strains), human and fowl cells less often (62 strains each) and less frequently rat cells (50), rabbit (28) and sheep cells (18). Human cells alone were agglutinated by 34 strains—the largest number of strains agglutinating only one cell type.

Only 51 of the 164 haemagglutinating strains belonged to the first 25 O groups of *E. coli* serotypes and haemagglutination did not appear to be associated with any particular O antigen. It is considered doubtful whether the haemagglutinating property is associated with pathogenicity. *J. Nagington*

KARAKASEVIC, B. Agglutininnachweis in den Faezes an infektiöser Colienteritis erkrankter Säuglinge und Kleinkinder. [**The Demonstration of Agglutinins in the Faeces of Infants and Children suffering from Infectious Enteritis caused by** *E. coli*] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1958, July–Aug., v. 116, Nos. 1/2, 126–44, 7 figs. [29 refs.]

The author gives an account of tests on the faeces of 56 infants and small children suffering from infectious enteritis, as proved by bacteriological and serological tests, who were treated with antibiotics. 28 infants and 21 small children who did not suffer from intestinal disturbance but were admitted to the clinic for other non-infectious diseases were taken as controls and their stools examined. [These are the figures from

the text. The summary gives the number of controls as 50.]

The results are summarized as follows:—

1. Agglutinins against various intestinal bacteria were demonstrated in the faeces of 22·0% of healthy infants and children; in 10% of the cases agglutinins against "dyspepsicoli bacteria" were found. Dyspepsicoli bacteria were cultured from stools in 2 cases (4%). A specific coproagglutinin was obtained only from 1.

2. Specific and unspecific agglutinins were isolated from the faeces of 82·1% of infants and children suffering from infectious enteritis. In 10·8% of the cases only specific, in 52·1% specific and unspecific, and in 36·9% only unspecific agglutinins were found. Coproagglutinins against dyspepsicoli bacteria were demonstrated in 51·7% of cases. In the cases in which specific and unspecific or only unspecific agglutinins were found, agglutinins against a non-pathogenic *E. coli* and against several varieties of enteropathogenic bacteria were demonstrated.

3. In the faeces of 7 children suffering from infectious enteritis anti-K (B) agglutinin against dyspepsicoli bacteria was found in low titre.

4. The specific agglutinin in the faeces of children suffering from infectious enteritis reached its maximum between the 5th and 8th days of the disease. The antibody had disappeared from the faeces in most cases on the 30th day. The non-specific agglutinin increased during the first days of the disease more quickly than the specific and appeared in higher titre; it remained in the faeces 40–60 days longer than the specific agglutinin.

5. In some cases it appeared that antibiotics suppressed the formation of coproagglutinins.

6. While coproagglutination as a diagnostic method for infectious enteritis requires further and systematic investigation, it can even now be of considerable assistance.

7. Demonstration of a specific agglutinin in the faeces of children suffering from infectious colitis gives further support to the pathogenicity of dyspepsicoli bacteria.

P. A. Clearkin

NISMAN, B. & HIRSCH, Marie L., with the technical collaboration of Anne M. BERNARD. Étude de l'activation et de l'incorporation des acides aminés par des fractions enzymatiques d'*E. coli*. [**Study of the Activation and Incorporation of Amino-Acids by the Enzymatic Fractions of** *Escherichia coli*] *Ann. Inst. Pasteur.* 1958, Nov., v. 95, No. 5, 615–36, 1 fig. [21 refs.]

YANOFSKY, C. **Restoration of Tryptophan Synthetase Activity in** *Escherichia coli* **by Suppressor Mutations.** *Science.* 1958, Oct. 10, v. 128, 843–4.

NIKLOWITZ, W. Mitochondrienäquivalente bei *Escherichia coli*. [**Mitochondria Equivalents in** *Escherichia coli*] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 173, Nos. 1/2, 12–24, 20 figs. [38 refs.]

WEBB, M. **Aminopterin Inhibition in** *Aerobacter aerogenes:* **Alanine and Valine Accumulation during the Inhibition and their Utilization on Recovery.** (With an Addendum on a Factorial Experiment to Study Factors which reverse Aminopterin Inhibition by J. D. BIGGERS & M. WEBB, 487–9, 1 fig.) *Biochem. J.* 1958, Nov., v. 70, No. 3, 472–86, 2 figs. [Numerous refs.]

EDWARDS, D. C. **Production of High-Titre Diphtheria Toxin in Baffled Shake Flasks.** [Correspondence.] *Nature.* 1958, July 19, v. 182, 190–91.

The author compared the production of diphtheria toxin on tryptic and papain digest media in shaken flasks provided with baffle plates fused into the bottom of the flask, with toxin production in the same conditions but in plain flasks [this *Bulletin*, 1948, v. 23, 207].

It has been found that the toxin production is much better in the baffled flasks and could reach a high level within 48 hours, much in the same way as it has been obtained with larger amounts of fluid incubated in aluminium tanks [*ibid.*, 1956, v. 31, 667] and stirred at 1,400 r.p.m. The addition of traces of detergent increases the yield in the baffled flasks but not in the tanks. It is suggested that this may be explained by the increased foaming in the flasks plus detergent which is similar to that produced in the tanks by high speed stirring.

It would seem, therefore, that the production of toxin is closely dependent on the phenomena of oxidation which are going on in the culture. *J. W. McLeod*

MARKS, J. & THOMAS, C. H. H. **Notes on the Cultivation of Tubercle Bacilli.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1958, Aug., v. 17, 194–202.

In this investigation, 1 ml. quantities of 40 specimens of microscopically positive sputa were mixed with 9 ml. of N NaOH for periods of time ranging from 10 to 60 minutes, after which the mixtures were immediately neutralized with phosphate buffer *p*H 7·0 and cultured. Exposure for 20 minutes produced less colonies than exposure for 10 minutes, and neutralization was shown to be unnecessary when buffered medium was used. This buffered medium was an egg medium [the formula is given in detail] and on it tubercle bacilli grew at the same rate as in Löwenstein-Jensen medium; of 503 specimens treated with NaOH and cultured after neutralization on Löwenstein-Jensen medium and without neutralization on the buffered medium, 56 specimens were positive on both media, 11 only on the Löwenstein-Jensen medium and 14 only on the buffered specimen. In a further comparison, 5,593 specimens of sputum were cultured at random on the 2 media; of the 2,800 neutralized specimens on the Löwenstein-Jensen medium, 221 were positive, and of the 2,793 un-neutralized specimens cultured on buffered medium, 223 were positive.

The value of incorporating 60 units penicillin per ml. into the medium before inspissation was also explored.

Of 2,673 specimens inoculated on to slopes, with and without the antibiotic, there were 162 positive cultures in both media, 22 positive only on the control medium and 45 only on the penicillin medium. Both cultures were contaminated in 17 cultures, the penicillin slope alone in 39 and the control slope alone in 155.

The effects of a number of modifications of Löwenstein-Jensen media were also examined. Omission of the starch had no effect in growth on freshly prepared medium but on aged medium its presence appeared to be an advantage. The presence of asparagine and citrate appears to be unnecessary but magnesium sulphate is of some value in the buffered medium. The addition of an ether-ethanol extract of tubercle bacilli which promotes growth on alkaline serum agar [this *Bulletin*, 1954, v. 29, 871] gave no benefit.

The origin of negative cultures from film-positive sputa was also investigated and the result showed that they mainly occurred just before conversion to the bacteriological negative state during therapy. The failure of the addition of PAB to the medium to decrease the proportion of these negative cultures indicates that the failure of the tubercle bacilli to grow is not due to residual PAS in the inoculum.

In an appendix to this paper, a detailed description is given for culturing sputum and gastric juice. Essentially the method for sputa consists of adding 2 ml. of sputum to 2 ml. N NaOH, shaking and inspecting at intervals up to 30 minutes, diluting with 18 ml. distilled water as soon as homogenizing is complete, centrifuging for 20 minutes at r.c.f. [relative centrifugal force] 1,200 and culturing on the buffered medium. Procedures are recommended for minimizing the risk of infection from aerosol formation, etc., to the worker. The recommendations for gastric secretion are that the specimen should be collected into an equal volume of 10% NA_3PO_4 $12H_2O$. After centrifuging, N NaOH is added and the specimen treated in the same way as sputum. *S. R. M. Bushby*

BALL, G. D. **Trial of Kirchner's Medium for Routine Isolation of** *Mycobacterium tuberculosis*. *Tubercle*. 1958, Aug., v. 39, No. 4, 242–6.

In this trial Kirchner (K) fluid medium was compared with Löwenstein-Jensen (L-J) medium during the culturing of 1,222 specimens from tubercle bacilli. The specimens of sputum, urine and pus were treated with 5% oxalic acid and centrifuged. Deposit from each specimen was inoculated into 1 tube of the Kirchner medium and on to 2 tubes of the Löwenstein-Jensen medium; the cultures were incubated for 5 weeks and the presence of tubercle bacilli was confirmed by staining. In the fluid medium the bacilli grew in "corded" white clumps at the bottom of the tubes.

The following table shows some of the results.

TABLE I

	No.	L-J+ K+	L-J+ K−	L-J− K+
Sputum	911	83	20	18
Urine	127	4	1	4
Pleural fluid	40	2	1	0
Others	44	2	0	0

Of the 39 microscopically positive sputum specimens, 37 were positive on both media, 1 was positive on the Kirchner medium and negative on the Löwenstein-Jensen medium and 1 was *vice-versa*.

The distribution of positive cultures between 1 or 2 Löwenstein-Jensen slopes and the Kirchner culture was determined on 91 positive specimens.

TABLE II.—DISTRIBUTION OF CULTURES FROM 91 POSITIVE SPECIMENS

Löwenstein positive				Kirchner positive	
	Both slopes	One slope only	Total		Total
K+	51	5	56	L-J+	56
K−	10	8	18	L-J−	17
Total	61	13	74	Total	73

The incidence of contamination was 8·5% in the Kirchner medium (mainly moulds) and 1–2% in the Löwenstein Jensen slopes. Although the use of 1 tube of Kirchner medium gave results equal to 2 tubes of Löwenstein-Jensen medium, the use of Kirchner medium is open not only to the criticism that the hazard of infection to the worker is greater than with with solid medium, but also to the facts that atypical strains are not recognizable by their pigmentation, the growth of tubercle bacilli is not always obvious to the naked eye and the contamination rate is high. Most of these criticisms could be overcome by using a tetrazolium salt, incorporating a low concentration of agar and adding a fungicide. *S. R. M. Bushby*

MIDDLEBROOK, G. & COHN, M. L. **Bacteriology of Tuberculosis: Laboratory Methods.** *Amer. J. Pub. Health.* 1958, July, v. 48, No. 7, 844–53. [10 refs.]

Maintaining that effective chemotherapy has increased the need for accurate bacteriological examination, the authors have compared the efficiency of two methods of preparing sputum for cultivation and of 3 media for growing the tubercle bacilli.

The two methods of preparation were the classical sodium hydroxide method and a digestion method. In one, a volume of sputum was treated with an equal amount of N NaOH at 37°C. for 30 minutes, centrifuged and the deposit washed in 0·1 M sodium citrate. In the other method, the sputum was first digested with trypsin for 60 minutes in the presence of $NaHCO_3$, centrifuged and the deposit then treated with 0·05 M sodium citrate and 0·25 N NaOH at 40°C. for 20 minutes, after which it was again centrifuged. In both methods the deposits were stained and the inocula diluted so as to yield isolated colonies. The results on 7 sputa show that the digestion method yielded from 2 to 16 times as many tubercle bacilli; one of the sputa contained the "yellow bacilli" and these were affected less by the stronger alkali method than were the tubercle bacilli.

The three media used were Löwenstein-Jensen (L-J)

medium, an oleic-acid-albumin solid agar (7H–10) and a similar but commercially available oleic-acid-albumin medium (7H–9). The 7H–10 medium was used in Felsen plates and the other 2 media as slopes in tubes. The plates were read after 3 weeks' incubation and the tubes after 3, 4, 5 and 6 weeks, the plates being incubated in polyethylene plastic bags permeable to CO_2 in a chamber to which 2–5% CO_2 was added daily; the tubes were incubated with their caps screwed down tightly. In the first study, 100 specimens of sputum were cultured and 86% were positive, 80% being positive on both 7H–10 and L-J, 3% being positive on 7H–10 but negative on L-J, and 2% being positive on L-J but negative on 7H–10. Growth on the 7H–10 medium was more rapid than on the L-J for whereas 83 specimens were positive on 7H–10 after the 3 weeks' incubation, only 77 were positive on the L-J at that time. Contamination rates on these 2 media were not significantly different (3% on L-J and 1·5% on 7H–10). Growth on 7H–9 was slower than on 7H–10 and even after 6 weeks' incubation the amount of growth was less than after the 3 weeks' incubation on 7H–10.

This paper also includes some comments on the bacteriological studies of 266 specimens from 100 patients, collected over a 7-month period during active chemotherapy. At least 100 colonies were grown on the 7H–10 medium from 90% of the smear-positive specimens, and from every patient at least 1 positive culture was obtained during the first week in hospital. In 95% of the patients, 2 positive cultures could be expected when a positive smear was obtained. "Yellow bacilli" were obtained from 2 patients, and these were easily identified by their strong catalase reaction and by their turning yellow on exposure to light for 18 hours.

Observations were also made on the determination of sensitivity of the primary inoculum to the anti-tuberculous drugs. Media containing concentrations of 0·2 μgm. isoniazid per ml., 2·0 μgm. streptomycin per ml. and 2·0 μgm PAS per ml., respectively, were placed in 3 of the quadrants of the Felsen plate, and the authors claim that 90% of the cultures yielding 100 colonies on the control quadrant give information of clinical value on sensitivity within the 3-weeks' period of incubation. *S. R. M. Bushby*

MARSHALL, J. **The Effect of Contamination on Löwenstein-Jensen Medium.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1958, Aug., v. 17, 202–6.

During incubation a proportion of Löwenstein-Jensen slopes show a change from the greenish-yellow colour to a bluish-green. This change is associated with contamination by Gram-positive cocci which lower the *p*H of the medium by fermenting the starch and thus producing the change in colour, and although the growth is often limited to one small area the whole of the slope changes in colour. Tubercle bacilli have been shown to be unable to grow in media showing this change.

In this paper experiments are described in which tubes of Löwenstein-Jensen medium, with and without malachite green, and tubes of Dorset egg medium, were heavily inoculated with H37Rv and deliberately infected with the contaminants (mainly streptococci) from routine cultures. The results showed that although growth of the tubercle bacillus was inhibited on most of the slopes, the inhibition was always greatest in the presence of the dye. The author suggests that this is due to the dye being more soluble and bacteriostatic in its dissociated form under the acidic condition.

The practical conclusion of this investigation is that any tube which shows this change will be contaminated, although the contaminant may not be readily visible, and therefore the specimen should not be regarded as containing no viable tubercle bacilli.

S. R. M. Bushby

GALE, D. **The Control of Contamination in the Cultivation of Tubercle Bacilli. I. An Overlay medium.** *Amer. J. Clin. Path.* 1958, Aug., v. 30, No. 2, 177–80. [10 refs.]

This overlay medium is produced by inspissating 5·5 ml. of ATS medium over a slope of 10 ml. of 2% agar in a 150 × 25 mm. tube. The agar contains 1 : 1000 Zephiran, added before autoclaving the agar, and 1·0 mgm. cycloheximide (Actidione) per ml., added at 50°C. before dispersion into the tubes and sloping. The agar is thus a reservoir for the antibacterial and antifugal agents which then diffuse into the egg medium; it also replaces the more expensive medium beneath the surface of the slope which contributes nothing to the growth of the tubercle bacilli.

2,486 specimens after treatment with caustic soda were inoculated on this medium and on normal ATS medium. In all, 768 specimens grew contaminants, 366 occurring on the normal ATS medium with no contaminants on the corresponding overlay medium, as compared with 86 on the overlay medium without contamination on the corresponding ATS medium. The remaining 316 grew contaminants on both media. Of the specimens, 323 were positive, 178 being positive on both media, 59 on the overlay medium but not on the ATS, and 86 on the ATS medium but not on the overlay medium. 43 specimens were positive on the overlay medium where the ATS medium was contaminated. *S. R. M. Bushby*

RAMAKRISHNAN, T., INDIRA, M. & SIRSI, M. **A New Growth-Factor for** *Mycobacterium tuberculosis.* *J. Indian Inst. Sci.* 1958, Apr., v. 40, No. 2, 15–22 (Sect. A.), 3 figs. (2 on pl.) [16 refs.]

In a preliminary note [this *Bulletin*, 1957, v. 32, 1099] the authors drew attention to the stimulating action of the water of tender coconuts on the growth of tubercle bacilli. The authors now report that the water, removed aseptically and added to the Youmans medium in concentrations as low as 1 : 10,000, enabled maximum growth of H37Rv to be obtained in 12 days instead of 21 days. Similar results were obtained on an egg medium to which the water was added before the coagulation of the medium.

Chemical fractionation of the constituents of the water into lipids, amino-acids, polysaccharides and a residue, showed that the activity lay in the polysaccharide fraction. The active principle resists autoclaving at 15 lb., and is soluble in dilute acids but not in water. Studies in mice showed that the factor did not affect virulence, and when the factor was administered intraperitoneally to mice infected with H37Rv, there was no evidence of stimulated growth of the organisms—in fact, in doses of 0·5 gm. per kgm. it increased the survival rate of the mice.

Attempts are being made to determine the chemical structure of the active substance. *S. R. M. Bushby*

MELVIN, Irene G. & MAC VANDIVIERE, H. **The Titration of Cord Formation as related to Virulence of Mycobacteria.** *Amer. Rev. Tuberculosis.* 1958, July, v. 78, No. 1, 83–92, 3 figs. [11 refs.]

The procedure used in this work involves 2 principles: 1, the use of human plasma to stabilize the process of cord-formation, and 2, the use of Tween 80 to disperse the cords or prevent their formation in liquid media. In practice, inocula of the tubercle bacilli from Dubos medium were grown in Dubos medium containing concentrations of Tween 80 ranging from none to 0·110% at 0·005% intervals and 5% human serum from human blood 22–29 days old, and after 7 and 14 days stained smears were examined under low power magnification for cording. The cord-formation titre was interpreted as the highest concentration of Tween 80 in which cording was discernible.

Of the human strains examined, H37Rv and a recently isolated strain gave titres of 0·11%, the attenuated strain, R1Rv, 0·07%, and the avirulent strains, R1Ra and H37Ra, less than 0·01%. Of the bovine strains, Ravenel gave a titre of 0·09%, and 4 BCG strains titres ranging from 0·01 to 0·05%. The variation in the titres of these BCG strains corresponded with their antigenic value, assessed by duration of allergy.

The pattern of the cording of the attenuated strains was similar to that of the virulent strains except that the cords were shorter and less compact.

A virulent avian strain showed no cording and the virulent bovine strain, Copenhagen, formed cords in concentrations up to 0·06% during incubation for 7 days but after 14 days' incubation the cords had dispersed.

The authors emphasize that a standard technique must be used if titres of different strains are to be compared, especially as the size of the media tubes affects the results. *S. R. M. Bushby*

BOWMAN, B. U., Jr. **Quantitative Studies on some Mycobacterial Phage–Host Systems.** *J. Bacteriology.* 1958, July, v. 76, No. 1, 52–62, 10 figs. [21 refs.]

The object of this paper is to present standard quantitative bacteriophage techniques for establishing such undefined characteristics as adsorption behaviour, latent period, and burst-size of the mycobacterium-phage system; the techniques are described in detail. The study was made on the D29 phage, with *Mycobacterium butyricum* for the propagation and assay of the phage and the avirulent strain ATCC No. 607 of *Myco. tuberculosis* and *Myco. ranae* for studies of the infectious processes. The parent phage produced 3 types of phage, which bred pure after 3 transplants; 2 of the types were used in this study, D29L and D29S, producing plaques 3–4 mm. and 2 mm. in diameter, respectively.

The soft-agar overlay technique was used for the phage counts, and the optimum quantities of medium were 2–3 ml. for the top layer and 25–30 ml. for the bottom in 90 mm. dishes; the size of the bacterial inoculum was not critical. Adsorption studies with D29S showed that the rate of adsorption was not exponential, there being a decrease with time. Further studies with the residual, unadsorbed phage suggested that the type was heterogeneous, consisting of fast and slow adsorbers, but whether the differences were genetic or phenotypic was not determined. Although additional calcium (5×10^{-4}M.) did not affect adsorption, in its absence abortion occurred, *i.e.* some of the phage particles failed to develop phage after adsorption. Similar experiments on 607 showed that the phage population was heterogeneous in adsorption rates, but with this type, adsorption was affected by excess calcium; abortion also occurred but it was unaffected by supplements of calcium, magnesium or manganese.

With the tubercle bacillus, adsorption of D29L was faster than of D29S and the proportion of slow-adsorbing phages was less in D29L than in D29S (15 and 40% respectively). Abortion also occurred and plating at various intervals showed that this increased with time; calcium did not affect the aborting. Adsorption of this phage by *Myco. ranae* was not studied in detail.

Significant adsorption of either phages by *Myco. butyricum* did not occur although this organism was used for the phage counts, but the failure may have been due to the effects of Tween 80 in the medium used for the growth of this organism.

Several preliminary one-step growth experiments did not give the sharp levelling or plateau effects produced by single bursts as in classical one-step growth results; instead a gradual two-step or three-step growth occurred, which could, however, have been due to the clumped state of the bacilli.

Neutralization tests with antisera prepared against each of the phages showed cross reactions and electron micrographs revealed no morphological differences between the phages. *S. R. M. Bushby*

ACHARYA, B. K., SULLIVAN, F. M. & ROBSON, J. M. **Immunity in Experimental Tuberculosis.** *Amer. Rev. Tuberculosis.* 1958, Aug., v. 78, No. 2, 203–25, 7 figs. [20 refs.]

In these experiments the challenge dose of tubercle bacilli was injected intracorneally into groups of mice according to the technique described by REES and ROBSON [this *Bulletin*, 1950, v. 25, 790]. The immunizing dose was usually injected intracorneally into the other eye, but in some of the experiments it was injected intradermally. Immunity was assessed by the percentage of animals in the group failing to develop a corneal lesion from the challenge dose. The results

are described under 3 headings; the effect of the time interval between immunizing and challenging doses on the development of immunity, the effects of varying the sizes of the immunizing and challenging doses, and the production of immunity with organisms killed by different methods. Alterations in the number of bacilli in the lesions were estimated under low-power magnification [ROBSON and SULLIVAN, this *Bulletin*, 1957, v. 32, 992].

Experiments in which groups of 6 mice were inoculated intradermally with 0·01 ml. of 10^{-3} dilution of a Dubos culture of a bovine strain and then challenged at 0, 1, 2, 3, 4, 5, 7 and 15 days and at 1, 3 and 6 months with 500 viable units showed that there was some immunity after the 2nd day and that it continued to develop rapidly during the 1st week and persisted for at least 6 months. When the animals were killed 7 months after vaccination, acid-fast bacilli were found in occasional compact masses but in animals re-inoculated after a 1-month interval no acid-fast bacilli were found in 2 corneas, and 3 showed only a few degenerated bacilli.

In an experiment in which immunizing doses were injected intracorneally and consisted of undiluted and 10^{-3} dilutions of the culture and in which the challenge doses consisted of 10^{-1}, 10^{-2} and 10^{-3} dilutions given to sub-groups at 1, 2, 4 or 8 weeks, only the 10^{-1} challenge dose produced lesions, which indicates that this large inoculum broke through the immunity shown against the smaller doses. There was some indication that better immunity was produced by the larger immunizing dose and that the immunity increased as the interval between immunizing and challenging increased to 4 months. In a second experiment in which the range of vaccinating doses was extended, the smaller inoculum gave the better protection but as in neither experiment was the difference statistically significant, the effect of varying the vaccination dose is not striking. However, in this experiment it was again shown that if the challenge dose is large it can break through the protection. Histological examination did not reveal the mechanism of the break-through for there was no evidence of increased extracellular multiplication of the bacilli or of decreased cellular activity.

Experiments with killed vaccine showed that heat-killed bacilli were less effective than those killed with alcohol or phenol, the best effects being obtained with the latter agent.

The authors are unable to explain the very rapid development of immunity in the experiments in terms of the classical concepts of immunity, and unsuccessful attempts to immunize against the tubercle bacillus with a variety of organisms, such as *Escherichia coli, Pseudomonas pyocyanea* and the pneumococcus, suggest that the effects are due to a specific action.

S. R. M. Bushby

GRAY, D. F. & AFFLECK, Margaret N. **Relationship of Allergy to Gross Lung Disease and Culturable Bacilli in Tuberculous Mice.** *Amer. Rev. Tuberculosis.* 1958, Aug., v. 78, No. 2, 226–34.

The experiments of this paper were designed to determine whether a relation could be demonstrated between the pre-allergic, allergic and terminal anergic phases of tuberculosis in mice, and the degree of activity of the tuberculous process in the lungs. The mice were infected intranasally with H37Rv with either 500 or 12,500 viable units, and the allergic state was assessed by injecting 1 : 25 OT into the foot; hyperaemic swelling 48 hours after the injection was regarded as evidence of allergy and the tests were done weekly. The gross lung changes were assessed by the increase in weight of the organs and viable counts were made on pooled lung tissue of the groups of animals.

The pre-allergic period lasted for 4–8 weeks depending largely on the size of the infecting dose, and it was characterized by a rapid increase in lung tissue and in the viable count; these changes culminated either in death or arrest of the disease. When the animals entered the allergic phase the extent of the disease was approximately the same irrespective of the size of the infecting dose, the degree of lung consolidation being less than in the pre-allergic phase, and during this phase the activity of the disease and the number of bacilli remained stationary. The anergic phase was associated with a fresh period of progressive increase in the disease process and the number of bacilli increased up to 1,000 times those present during the allergic phase.

Early death of mice receiving the larger infecting dose was associated with a failure to develop the allergy and in consequence the lung consolidation and the increase in bacilli continued unchecked. *S. R. M. Bushby*

GRAY, D. F. **Immunity, Natural Anergy, and Artificial Desensitization in Experimental Tuberculosis.** *Amer. Rev. Tuberculosis.* 1958, Aug., v. 78, No. 2, 235–50, 1 fig. [15 refs.]

This paper is a continuation of the previous one [above] in which tubercle bacilli in mice were shown to increase during the pre-allergic phase of the disease, remain stationary in number during the allergic phase and then to increase rapidly again during the terminal anergic phase of the disease. In the present paper the observations were extended to guineapigs.

In the first experiments, 11 of these animals were infected intranasally with 5,000 bacilli and 6 of them died while still tuberculin-positive, but their physical condition was either fair or good and they were considered to have died from a prematurely fatal complication, *e.g.* ruptured spleen or liver; the number of bacilli in the lungs ranged from 9·7 million to 160 million. The other 5 guineapigs were in an anergic state when they died, having become insensitive to tuberculin 2–4 weeks previously. They were ill and emaciated, and the number of bacilli in their lungs ranged from 1,150 million to 22,000 million.

In a second experiment 26 guineapigs were infected intranasally and 16 of them were treated with OT. The dose of OT was 0·2 ml. rising to 1 ml. daily after 1 week and reduced to 1 ml. every 3 days after the 8th week; in 5 animals the treatment was stopped after 5 weeks. The animals given the continuous treatment remained tuberculin-negative throughout the 16 weeks' period of the experiment but 3 of the 5 receiving the

short course of treatment became strongly positive 8–10 weeks after the treatment was stopped and the other 2 became weakly positive at the end of the experiment. Some untreated animals and some receiving the continuous treatment were killed 4 and 6 weeks from the day of infection, and less rapid spread of the disease was present in those rendered tuberculin-negative by the tuberculin treatment than in the untreated animals, although no significant difference was found in the number of bacilli in the lungs. The arrest of bacillary multiplication seen in allergic mice was also seen in these guineapigs but, as it was also seen in the desensitized animals, this artificial state of anergy must be different from the natural one of the terminal stage of the disease. The less rapid spread of the infection in the tuberculin-treated animals showed that they had retained their immunity and suggests that the allergic state in the untreated animal aided the spreading of the disease.

A similar desensitization experiment was also made in mice and, although in these animals the tuberculin-negative state was again shown to differ from the natural anergic state, the suppression of bacillary multiplication being maintained in spite of the mice being tuberculin-negative, there was little evidence that the tuberculin treatment affected the course of the disease.

The author postulates the existence of 2 separate hypersensitive states, both of which are detected by tuberculin; the first can be suppressed by tuberculin and is associated with the phenomenon of allergic damage, and the other is not affected by tuberculin, although its reactivity to cutaneous tuberculin is suppressed and may be related to a specific immune change in the phagocytes. *S. R. M. Bushby*

BURRELL, R. G. & RHEINS, M. S. **Production of Anti-Lung Substances in Rabbits by Homologous Tuberculous Tissue Antigens.** *Amer. Rev. Tuberculosis.* 1958, Aug., v. 78, No. 2, 259–67, 1 fig.

The object of the experiments described in this paper was to determine the factors that might influence the production of antibodies to the host's tissues in tuberculosis; the experiments were made in rabbits.

The sensitizing antigens were homogenized lungs of healthy and tuberculous rabbits, and the antigen for the serological test was normal lung tissue disintegrated by ultrasonic vibration. The natural antibodies in the test sera were destroyed by heating at 65°C. for 25 minutes.

In the first experiment 5 rabbits were immunized with normal lung antigen and 8 with tuberculous lung antigen, and bled at weekly intervals. No complement-fixing antibodies for the normal lung antigen or agglutinating antibodies for red cells coated with tuberculosis were detected in the animals injected with the normal lung tissue during the 6 weeks' observation period, but antibodies with titres of 1 : 2 to 1 : 64 to both these antigens were detected in those injected with the tuberculous tissue. Some of the sera showed high anti-complementary activity and as this may have been due to circulating antibody-lung-antigen complexes, the sera were tested for the antigen by mixing the sera with a mineral oil adjuvant and injecting them into rabbits; antibodies from lung tissue were detected, confirming that the lung antigen was present in the original serum.

In further experiments it was shown that injecting the antigen intravenously, intramuscularly or subcutaneously gave inferior antibody titres to those obtained by intraperitoneal injection. Injecting normal lung tissue with adjuvants and tubercle bacilli produced the same quantitative response as 6 times the quantity of tuberculous lung tissue without adjuvant. Tuberculous tissue without tubercle bacilli in the adjuvant gave the same response as the normal tissue plus tubercle bacilli.

In attempts to identify the factor in tuberculous tissue responsible for this antibody to lung tissue response, rabbits were injected with a mixture of lung tissue and tuberculin and the negative response indicated that the factor was associated with the whole bacillus. The antibodies for lung tissue were specific, for although the sera reacted with other tissue antigens, these could be removed by absorption with acetone-extracted kidney sediment, and cross-adsorption with lung tissue and tubercle bacilli showed that the lung antibodies were distinct from the tuberculous antibodies.

As these experiments show that the tuberculous infection *per se* is not essential for the production of these antibodies, it is therefore likely that the antibody production is related to the tissue response initiated by the bacillus, and this explanation is in keeping with the generally accepted concept that tubercle bacilli enhance the host's response to a variety of antigens.
S. R. M. Bushby

PITAL, A., PITAL, Ruth C. & LEISE, J. M. **A Rapid Method for determining the Drug Susceptibility of *Mycobacterium tuberculosis*.** *Amer. Rev. Tuberculosis.* 1958, July, v. 78, No. 1, 111–16. [Refs. in footnotes.]

This note describes experiments in which heavy inocula (2 loopfuls from solid medium per 75 ml.) of H37Rv and H37Ra are grown in Dubos medium for 24 hours and then distributed into flasks containing filter paper disks impregnated with known quantities of dihydrostreptomycin or isoniazid. After 4 days' incubation with the streptomycin or 7 days with the isoniazid, 0·7 ml. of 0·05% resazurin per 5 ml. of medium was added, and after 5 hours' incubation the colour of the dye was noted. In medium in which the drug had not affected the metabolism of the bacilli the dye changed to purple and finally to pink; in the medium in which the drug had a slight inhibitory effect the purple colour persisted. The results show that the metabolism of both strains was affected by 6 μgm. of streptomycin or isoniazid per ml. but not by 0·06 μgm. of the drugs per ml.; these concentrations corresponded to the sensitivities of the strains, determined by the usual tube dilution method.

A different pattern of interference was noted between the 2 drugs; with streptomycin the inhibition by 6·0

and 12 μgm. per ml. was persistent, whereas inhibition by these concentrations of isoniazid was transient, reflecting different modes of drug action.

With this method the authors claim that the sensitivity of a strain can be determined within 5 or 8 days respectively of obtaining sufficient growth on the primary medium to yield the 2-loopful inoculum.

S. R. M. Bushby

MITCHISON, D. A., SELKON, J. B., HAY, D., STEWART, Sheila M. & WALLACE, A. T. **Solid and Liquid Medium Tests of Streptomycin Sensitivity of** *Mycobacterium tuberculosis*. *Tubercle*. 1958, Aug., v. 39, No. 4, 226–31.

One of the authors had previously reported that some strains of tubercle were resistant to streptomycin when tested on Löwenstein-Jensen medium but were sensitive when tested in Dubos liquid medium [STEWART, this *Bulletin*, 1956, v. 31, 78]. In the present paper the results are reported of examining 36 cultures from patients who had had no treatment with streptomycin and 84 cultures resistant or possibly resistant to streptomycin. The examinations were made in 2 hospitals in Edinburgh and 1 in London, Löwenstein solid medium and Dubos medium, with and without Tween 80 and with Triton WR1339, being used. The streptomycin was added aseptically to the liquid medium and to the egg medium before inspissation. The results are expressed as resistance ratios, H37Rv having been examined with each batch of cultures.

A resistance ratio of 8 or more on solid medium and 4 or more in the Tween medium was taken as denoting resistance, and no resistant strain was found among the expected sensitive strains, although a variation was noted in the minimum inhibitory concentration in the Löwenstein medium at the 3 hospitals; 2 μgm. per ml. and 8 μgm. per ml. were the concentrations in the Edinburgh hospitals, and 16 μgm. per ml. in the London hospital. Among the expected resistant strains, 80% were resistant on the solid medium, as compared with 62% in the Tween medium, thus confirming that the Tween medium is inferior to the egg medium. This difference was, however, more marked in Edinburgh, where 12 of the 40 cultures tested at both the hospitals were resistant on the solid but sensitive in the Tween medium, compared with 6 of the 44 strains tested in London. This larger difference in the media shown in the Edinburgh results was attributed to the Tween medium in Edinburgh being of relatively poor quality, although the cause was unknown.

The compounded results of the hospitals, with Dubos medium without a surface-active agent and with Triton, showed that these 2 media were of similar efficiency to the egg medium, although in Edinburgh the results favoured the solid medium, and in London the fluid medium.

The authors therefore conclude that the solid medium is superior to Dubos medium for these tests, but, as they strongly favour expressing the results in terms of resistance ratio, the concentrations of streptomycin in this medium should be so arranged that the critical values of 4–16 can be obtained. *S. R. M. Bushby*

TSUKAMURA, M. & NODA, Y. **The Mechanism of the Combined Effect of Antituberculous Drugs.** *Amer. Rev. Tuberculosis*. 1958, July, v. 78, No. 1, 121–6.

The mechanism of combined effects of antibacterial drugs can be considered in terms of effects on a single cell or on a bacterial population, and the purpose of the present paper is to observe the mechanism from these 2 points of view on H37Rv growing on Ogawa egg medium.

In determining the number of viable bacilli growing in the presence of the drugs, sets of tubes were inoculated with decreasing inocula and only those growing 150 or less colonies were counted. Thus, the probability that the population contained mutants was low and the variations in drug susceptibility were considered to be physiological variations occurring among cells of the same susceptible genotype. The drug concentrations used were not completely inhibitory, being 0·5 and 2·0 μgm. streptomycin per ml., 0·005 and 0·01 μgm. isoniazid per ml. and 0·05 and 0·1 μgm. PAS per ml., and the number of colonies developing after 5 weeks' incubation was determined for each of the drugs alone and in paired combinations.

The 95% confidence limits of the counts were calculated by assuming that if there is no interaction between the 2 drugs then the ratio of the number of colonies growing in the presence of both drugs could be expected to be a product of the ratio of the numbers growing in the presence of the single drugs. The results are given in tabular form and no statistically significant interaction is shown between the drugs, although there is a tendency for the ratios between PAS and streptomycin to be smaller than those expected, suggesting an interaction between these 2 drugs. There was no evidence of antagonism.

Effects on growth rates of single bacilli were estimated by measuring the size of the colonies. No effects were observed with isoniazid but the colonies growing in the presence of streptomycin and PAS were smaller than those growing in the absence of the drugs and the size was even further reduced when the drugs were in combination, suggesting an enhanced retardation of the growth rate although the difference was not statistically significant. The authors therefore suggest that the increase in the activity of mixtures of streptomycin and PAS result from the doubling of these retarding effects on growth rate. *S. R. M. Bushby*

PATNODE, R. A. & HUDGINS, P. C. **Effect of Kanamycin on** *Mycobacterium tuberculosis in vitro*. *Amer. Rev. Tuberculosis*. 1958, July, v. 78, No. 1, 138–9.

In modified Proskauer and Beck medium, 0·62 μgm. kanamycin per ml. inhibited the growth of the H37Rv, Ravenel and BCG strains of tubercle bacilli during 5 weeks' incubation. The addition of 0·5% bovine serum had no effect on the activity against the Ravenel and BCG strains but the inhibitory concentration against H37Rv was increased to 5 μgm. per ml.

S. R. M. Bushby

BARRY, V. C. & CONALTY, M. L. **Antituberculosis Activity in the Phenazine Series. II. N^3-Substituted Anilino*apo*safranines (Rimino-Compounds) and Some Derivatives.** *Amer. Rev. Tuberculosis.* 1958, July, v. 78, No. 1, 62–73, 1 fig.

The writers have previously reported on the antituberculous activity of anilino*apo*safranines and their isomers [this *Bulletin*, 1957, v. 32, 245], and in the present paper they are reporting the activities of 67 rimino compounds. These can be regarded as derived from the former compounds by substitution of the hydrogen of the imino-group in the 3rd position of the phenazine nucleus.

In mice infected with H37Rv, only 2 of the series showed no activity but the activity of the others varied widely, it being very high in 8. The compound with the highest activity and the one most extensively examined was B663, in which R and $R'' = C_6H_4Cl(p\text{-})$ and $R' = CH(CH_3)_2$; 20 mgm. per kgm. in the diet for 14 days increased the median survival time by >300 days (control mice died in 15–18 days), and 1 mgm. per kgm. increased the time by 15 days.

B663 is considered to be more active than any other compound yet described and it is highly active in experiments in which the treatment is delayed for 6 days. With this compound, crystals of the pure drug are deposited in the tissues and definite activity was shown when treatment was stopped 7 days before the day of infection; this protection is regarded as true chemoprophylaxis. Growth of H37Rv in Proskauer and Beck medium enriched with sera is inhibited by about 1·0 μgm. per ml., and no resistance developed after 17 subcultures; no resistant variants were isolated from mice infected with the Ravenel strain as long as 470 days after the cessation of treatment with this drug. The rimino-compounds were well tolerated by mice, guineapigs and rabbits.

11 glyoxalino-phenazines were also examined and these showed moderate activity, but 4 *apo*safranine compounds were inactive when fed in the diet at 200 mgm. per kgm. *S. R. M. Bushby*

FROELICH, E. J. **The Effect of 5-Heptyl-2-Thiohydantoin on Experimental Tuberculosis.** *Amer. Rev. Tuberculosis.* 1958, July, v. 78, No. 1, 74–82, 2 figs.

In mice infected intravenously with H37Rv, daily oral doses of 5-heptyl-2-thiohydantoin ranging from 150 to 600 mgm. per kgm. gave very definite protection, the median survival time of the treated animals being >31 days as compared with 19·5 days for the untreated controls, and the average pathological score ranging from 63·5 (150 mgm. per kgm.) to 23·0 (600 mgm. per kgm.) as compared with 91·5 in the control group; similar activity was shown against a streptomycin-resistant variant of H37Rv. Some activity was also shown against an isoniazid-resistant variant, but as this strain caused few deaths in the untreated animals the activity was assessed on the extent of the disease. No activity was shown against the bovine, Ravenel strain.

The drug also showed activity in hamsters, infected subcutaneously with H37Rv, in which the disease develops slowly but shows a marked predilection for the lungs. In groups of 40 of these animals treatment was started on the 3rd day after infection in 1 group and on the 21st day in another. The drug was given in the diet in concentrations of 0·1, 0·2 and 0·4% to subgroups of 10 hamsters, and the remaining 10 hamsters were given 0·4% PAS in the diet. On the 125th day, when half of the control animals were dead, the surviving animals were killed, and in the animals receiving the higher dose of the drug there was little evidence of the disease, even in those animals in which the treatment was delayed; the lowest dose (0·1%) also showed definite activity, its activity being of the same order as that produced by the PAS (0·4%).

In experiments in mice, in which the thiohydantoin was given in conjunction with sub-effective doses of dihydrostreptomycin (250 μgm. per day) and isoniazid (0·0015% in the diet), doses of 100, 200 and 400 mgm. per kgm. were superior to therapy with any of the drugs given alone.

The drug is well tolerated; the acute oral LD50 dose in mice is greater than 10 gm. per kgm., and daily doses of 100 mgm. per kgm. to dogs and 160 mgm. per kgm. to monkeys for 14 weeks produced no significant toxic effects. In a limited trial in tuberculous patients the author states, however, that the response has not been sufficient to justify the use of the drug as an alternative to isoniazid or streptomycin although it may offer an alternative to PAS in combination therapy. *S. R. M. Bushby*

BOJALIL, L. F., BASTARRACHEA, F., CERBÓN, J. & PÉREZ-TAMAYO, R. **Distribution of Tubercle Bacilli resistant to Streptomycin and Isoniazid within the Lung.** *Acta Tuberculosea Scandinavica.* 1958, v. 35, Nos. 3/4, 265–74. [11 refs.]

The purpose of this paper was to study the frequency of the appearance of resistant tubercle bacilli in relation to the type of tuberculous lesion and the distribution of resistant organisms in different pulmonary lesions. The data were obtained from 297 lesions from 91 surgical resections. Material from the lesions was cultured on Löwenstein-Jensen-Holm medium and sensitivity to streptomycin and isoniazid was determined on the primary culture. Cultures growing to the same extent in the presence of 1 μgm. isoniazid or 10 μgm. streptomycin per ml. as in the absence of the drugs, were regarded as of medium resistance and those growing to the same extent in 10 μgm. isoniazid or 100 μgm. streptomycin per ml. as fully resistant. The patients had been treated for at least 4 months with streptomycin and isoniazid.

Of the 297 lesions, 200 yielded positive cultures, and of the 159 tested for sensitivity, 24 were of medium resistance to streptomycin and 34 were fully resistant, but 37 were of medium resistance to isoniazid and 37 were fully resistant. This greater frequency of isoniazid-resistant strains was apparently not related to the site from which they originated, for of the strains from cavities, 32 were resistant to isoniazid and 27 to streptomycin, and of the strains from nodules, 28 were resistant to isoniazid and 17 to streptomycin. The

authors suggest that the greater frequency of isoniazid-resistance in cavities could be due to the inactivation of streptomycin by the high concentration of deoxyribonucleic acid in those lesions, leaving isoniazid as the only active agent, and in nodules there may be acidity or low oxygen tension which would affect the action of streptomycin but not that of isoniazid.

In 27 patients it was possible to relate the sensitivities of the organisms isolated from the sputum with those of organisms from the lesions. However, in many cases this relation did not hold with strains isolated from different lesions of the patient, and in others the resistance of the sputum bacilli seemed to be due to a combination of different strains from 2 or more cavities. In 9 of the 27 cases in which correlation was found, there were variations in the degree of resistance to both drugs among the strains isolated from different lesions, but in the other 18 cases the distribution of resistance was homogeneous. The authors believe that the nature of the lesion, as well as the physico-chemical environment, influence the unequal distribution of resistance.

S. R. M. Bushby

BLANC, M. Étude du *Mycobacterium marianum*. [**Study of** *Mycobacterium marianum*] *Maroc. Méd.* 1958, June, v. 37, No. 397, 650–67. [66 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 168.]

HILSON, G. R. F. & ELEK, S. D. **Intratesticular Multiplication of** *Mycobacterium leprae murium* **in Normal and Suramin-Treated Animals.** *Internat. J. Leprosy.* New Orleans. 1957, Oct.–Dec., v. 25, No. 4, Pt. 1, 380–91, 3 figs.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 168.]

HOLLINGER, Nell F. & LINDBERG, Lois H. **Delayed Recovery of Streptococci from Throat Swabs.** *Amer. J. Pub. Health.* 1958, Sept., v. 48, No. 9, 1162–9, 1 fig. [28 refs.]

From 1,603 persons pairs of throat swabs were taken; the swabs were made of Dacron. One swab was plated immediately; the other was held in a tube, with silica gel to hasten drying, for 2–10 days before plating. For 1,098 persons, one swab was made with serum-impregnated cotton-wool, the other with Dacron. The Dacron swab was first rubbed over a strip of filter paper enclosed in a protective foil, and then sent directly to the laboratory for plating. After 2–10 days the filter paper was cultivated by pressing it on to the surface of a blood agar plate.

For the comparison between immediate and delayed plating of the Dacron swabs there were 324 persons who had one or other swab positive for haemolytic streptococci. Both were positive in 199, the immediate only in 82 and the delayed only in 43. For the filter paper comparison there were 243 positives; 153 were positive by both methods, 25 were positive by immediate control swab and not by filter paper, and 65 by filter paper only.

R. E. O. Williams

ESSEVELD, H., DANIËLS-BOSMAN, M. S. M. & LEIJNSE, B. **Some Observations about the Camp Reaction and its Application to Human β Haemolytic Streptococci.** *Antonie van Leeuwenhoek: J. Microbiol. & Serol.* 1958, v. 24, No. 2, 145–56, 5 figs. [14 refs.]

Lancefield's group B streptococci can be recognized by the CAMP test [this *Bulletin*, 1945, v. 20, 233], that is their ability to produce clear haemolysis of sheep red cells previously treated with staphylococcal β-toxin. In the authors' experiments the staphylococcus was streaked in a line across a sheep-blood agar plate, and the cultures of streptococci under test inoculated at an angle of about 45° to it. Experiments indicated that the CAMP factor could not penetrate far into an agar zone containing β-toxin, though the reverse could occur.

Of 218 group B streptococci 205 were strongly and 12 weakly CAMP-positive; only 1 gave no reaction. Of 724 strains of groups C, F and G only 1 was positive and 1 weakly positive. On the other hand, 60 of 202 strains of group A were strongly positive and 101 were weakly positive. [cf. MUNCH-PETERSEN, CHRISTIE and SIMMONS, this *Bulletin*, 1946, v. 21, 268.]

Some preliminary chemical examinations suggested that the CAMP factor was probably a polypeptide.

R. E. O. Williams

MCCARTY, M. **Further Studies on the Chemical Basis for Serological Specificity of Group A Streptococcal Carbohydrate.** *J. Exper. Med.* 1958, Sept. 1, v. 108, No. 3, 311–23, 3 figs.

McCarty has previously shown that the dominant specificity of the group A carbohydrate of haemolytic streptococci is dependent on N-acetyl-glucosamine side chains [this *Bulletin*, 1957, v. 32, 498]. It has now been shown that muramic acid is not concerned in serological specificity. A number of azo antigens were prepared by coupling p-aminophenyl-β-*N*-acetyl-glucosaminide to egg albumin or serum albumin. These antigens gave good precipitin reactions with group A antisera prepared against whole streptococci, and none with antisera for the group A variant [*loc. cit.*] or other groups. However, no reverse cross-reaction could be obtained with antisera to the azo antigen and streptococcal carbohydrate. The azo antigens were able to inhibit specific precipitation and could induce the production by a soil bacillus of the enzyme that specifically destroys the group A carbohydrate. The enzyme was not able to liberate *N*-acetyl-glucosamine from the azo antigen.

R. E. O. Williams

LANCEFIELD, Rebecca C., with the technical assistance of W. N. EVERLY. **Occurrence of R Antigen Specific for Group A Type 3 Streptococci.** *J. Exper. Med.* 1958, Sept. 1, v. 108, No. 3, 329–41. [13 refs.]

There are 2 series of type-specific antigenic proteins in group A streptococci, known as M and T; only the M antigen is correlated with virulence and only M antibody confers specific protection on mice or specifically enhances the bactericidal power of blood. The M antigen is recognized by a precipitin test with an acid

extract of the cocci. About 50% of strains of type 3 have now been found to possess an additional protein antigen, extracted by hot acid, which differs from the M antigen in that its antibody does not enhance the bactericidal power of blood nor protect mice against infection with M-containing strains. Strains containing the new antigen but no M could be obtained by passage of the M containing strains in artificial media, and could be brought back to producing M by serial passage in mice.

By analogy with type 28, which possesses an acid-extractable protein antigen not associated with virulence [this *Bulletin*, 1958, v. 33, 173], the newly discovered antigen is referred to as an R antigen.

R. E. O. Williams

BARKULIS, S. S., WALSH, G. & EKSTEDT, R. D. **Studies of Streptococcal Cell Walls. II. Type-Specific Antigenicity in Rabbits.** *J. Bacteriology*. 1958, July, v. 76, No. 1, 109–15. [17 refs.]

The purified M protein of group A streptococci is only poorly antigenic although it retains its serological reactivity. In earlier work in this series [this *Bulletin*, 1958, v. 33, 275] the authors suggested that the type-specific antigenicity was a function of a larger fraction of the cell wall, or that the whole wall was necessary for the production of type-specific antibodies. The antigenicity of cell walls and whole cells was therefore compared.

2 strains of type 14 streptococci were used to prepare whole cell and cell-wall vaccines from the same number of cells. Their dry weight and nitrogen content were estimated, and the volumes were adjusted so that the cell-wall vaccine contained $\frac{1}{4}$ dry weight and $\frac{1}{6}$ nitrogen content of the whole cell vaccine.

3 immunization experiments were carried out, and this procedure and that of serum testing by quantitative precipitation tests, mouse protection tests and bactericidal tests are described in detail.

Quantitative precipitation tests showed that both vaccines stimulated the production of type-specific antibody, but levels were lower when cell walls were used. Immunization beyond the 4th week did not increase the level. Mouse-protection tests showed that roughly the same protection was obtained by sera produced by either vaccine although there was a large difference in their titre as judged by precipitation. Serum from 3 out of 4 rabbits in each group was bactericidal in volumes of 0·01 ml. and 1 of each group showed activity in a higher dilution.

All M protein is in the cell wall and since whole cells are more efficient at promoting antibody response, the authors conclude that the antigenicity is potentiated by other cellular components. They suggest that cell walls might be used for human immunization since whole-cell vaccines are not satisfactory. *M. Patricia Jevons*

HALBERT, S. P. **The Use of Precipitin Analysis in Agar for the Study of Human Streptococcal Infections. III. The Purification of Some of the Antigens detected by these Methods.** *J. Exper. Med.* 1958, Sept. 1, v. 108, No. 3, 385–410, 12 figs. on 5 pls. & 9 text figs. [35 refs.]

The author's thesis is that the recognition of streptococcal products by their reaction with antibodies in human sera—in this case pooled gamma globulin—certainly reveals those products that are produced when the streptococcus grows *in vivo*, and by inference those that are likely to be important in pathogenesis. Culture supernatants of streptococci were partially purified and then submitted to continuous-flow electrophoresis; the various fractions were adjusted to have the same protein content and were then set up in adjacent wells for a gel-diffusion test against pooled gamma globulin. By this means one strain of a group A streptococcus was shown to yield at least 12 distinct antigens. There was some evidence to show that particular precipitin-lines were attributable to streptolysin O, the group carbohydrate, diphosphopyridine nucleotidase, and the proteinase precursor. The results are described in some detail. *R. E. O. Williams*

OGBURN, C. A., HARRIS, T. N. & HARRIS, Susanna. **Extracellular Antigens in Steady-State Cultures of the Hemolytic Streptococcus: Production of Proteinase at Low pH.** *J. Bacteriology*. 1958, Aug., v. 76, No. 2, 142–51. [17 refs.]

2 strains of group A streptococci were grown in a chemically-defined medium in a chemostat; the supernatants were concentrated by pervaporation and dialysis and examined by paper electrophoresis and gel diffusion against rabbit antisera. Cultures grown at *p*H 6–6·3 contained 1 protein in relatively high concentration, and this was identified as the streptococcal proteinase. The results are presented and discussed in considerable detail. *R. E. O. Williams*

KELLNER, A., FREEMAN, Elizabeth B. & CARLSON, A. S. **Neutralizing Antibodies to Streptococcal Diphosphopyridine Nucleotidase in the Serum of Experimental Animals and Human Beings.** *J. Exper. Med.* 1958, Sept. 1, v. 108, No. 3, 299–309, 2 figs.

Many strains of group A haemolytic streptococci produce an enzyme (DPNase) that breaks down diphosphopyridine nucleotide. This enzyme has now been shown to be antigenic in rabbits, in which it stimulates the production of a neutralizing antibody (ASDA). Sera from 240 randomly selected hospital patients were tested for ASDA; 80% had titres of 50 units per ml. or less, and 10% had titres of 100 or more. Titres were of this order in the first 5 months of life and in adults, but were much lower in children between $\frac{1}{2}$ and 5 years of age. After known streptococcal infection the ASDA titre usually rose, about as soon as antistreptolysin O (ASO). There was not, however, complete correlation between the ASO and ASDA changes. ASDA titres sometimes increased after infection with streptococci of types not known to produce DPNase. *R. E. O. Williams*

KOHOUTOVÁ, M. **Effect of Monovalent Cations on Type Specificity Transformation in Pneumococci.** [Correspondence.] *Nature*. 1958, July 19, v. 182, 188–9. [10 refs.]

Type transformation of pneumococci by means of deoxyribonucleic acid was found to be more consistent

when the classical neopeptone anti-R serum broth had added to it salts with monovalent cations, such as dipotassium or disodium hydrogen phosphate. In the presence of such salts transformation occurred throughout the growth cycle, whereas in their absence it occurs best after the end of the logarithmic phase, and also to some extent before the log phase. The salts may function by affecting the permeability of the cell membrane. *R. E. O. Williams*

HENNESSEY, R. S. F. & MILES, R. A. *Staphylococcus aureus* **Type 80 and Human Infections in Uganda.** *Brit. Med. J.* 1958, Oct. 11, 893–5, 1 chart. [16 refs.]

248 strains of coagulase-positive staphylococci isolated from various routine cultures in 2 hospitals in Uganda between November 1955 and March 1957 were examined for phage type. Altogether 40% proved to belong to type 80. The type-80 strains were found in a great variety of lesions, both superficial and deep, among Africans, Asians and Europeans. 97% of the type-80 strains were penicillin-resistant and 31% were streptomycin-resistant; only 3% were tetracycline-resistant. *R. E. O. Williams*

KIENITZ, M. Zum Nachweis des Staphylokokken-Enterotoxins an der weissen Maus. [**The Demonstration of the Enterotoxin of Staphylococci in White Mice**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 171, Nos. 6/7, 451–6. [38 refs.]

Attempts were made to confirm the observations of LEGLER *et al.* (*Offentl. Gesundheitsdienst*, 1957, v. 19, 198) that mice form a suitable animal for detecting staphylococcal enterotoxin. No success was obtained, either by feeding or by injection of various preparations from a number of recognized enterotoxin-producing strains. *R. E. O. Williams*

VOGELSANG, T. M. **Carriage of Phage Patterns of Pathogenic Staphylococci in Medical Students.** *Acta Path. et Microb. Scandinavica.* 1958, v. 43, No. 2, 196–210, 2 figs. [26 refs.]

Nose, throat and skin swabs were taken from 42 medical students in Norway, starting on their return from holiday in an attempt to establish at what stage in their ward teaching they became infected with penicillin-resistant pathogenic staphylococci. 18 students (Class A) were examined weekly during their main bacteriological course of 10 weeks and 24 students (Class B) were examined during their preliminary bacteriological course of 3 weeks and continued in the main course after they had had 6 months in the wards.

More positive swabs were obtained from throat swabs than from nose swabs in both classes and only 55 strains in all were isolated from hand swabs, 7 coming from students who were not upper respiratory tract carriers. 40% of strains from Class A students and 13% of strains from Class B students were penicillin resistant. 22% of all strains were not typable by phage typing and of the remainder, strains of Group III predominated. There was evidence that some students acquired strains of several different types during the sampling period. All the penicillin-resistant strains belonged to Group III except one which belonged to Group I.

The author was unable to demonstrate significant changes in the crude carrier rate or the penicillin-resistant carrier rate during the sampling period but he stresses the importance of examining throat swabs in investigations of this type.

[For previous studies by the author, see this *Bulletin*, 1954, v. 29, 666, 772, 773.] *M. Patricia Jevons*

RAMSEY, H. H. **The Response of *Micrococcus pyogenes* to Low Concentrations of Chloramphenicol.** *Antibiotics & Chemotherapy.* New York. 1958, July, v. 8, No. 7, 338–41, 1 fig. [15 refs.]

A strain of *Staphylococcus aureus* was cultivated in broth containing 0, 5, 10 and 20 μgm. per ml. of chloramphenicol, and aliquots were plated on nutrient agar and on the same medium containing 10 μgm. per ml. of chloramphenicol at hourly intervals for 9 hours, colonies being counted. In the initial plating before incubation the proportion of resistant cells was small, colonies on chloramphenicol-containing medium amounting in no case to over 6·5% of those on normal medium. In broth containing 5 and 10 μgm. per ml. of chloramphenicol growth was retarded, but the proportion of resistant cells rose in 4 hours to over 90%. In 20 μgm. per ml. there was no increase at all in the total count, but the proportion of resistant cells rose to 45% in 9 hours. In antibiotic-free broth this proportion rose to 55% in 5 hours and then fell steeply. This change in resistance in normal medium is considered to be an effect of greater metabolic activity. That in antibiotic-containing medium must be an adaptive change: such an effect involving almost the whole population in a short period during which little multiplication occurred could not be the result of mutation. *L. P. Garrod*

CARRÈRE, L., ROUX, J. & SERRE, A. Antigènes des *Brucella*. I. Généralitiés. Étude des endo-antigènes et des antigènes glucido-lipido-polypeptidiques par les méthodes de diffusion en gel. [**The *Brucella* Antigens. General Considerations. Study of the Endo-Antigens, of the Glucidic-Lipidic-Polypeptidic Antigens, by means of Diffusion in Agar-Gel**] *Ann. Inst. Pasteur.* 1958, Nov., v. 95, No. 5, 588–603, 4 diagrams. [27 refs.]

The English summary appended to the paper is as follows:—

"*B. Melitensis, B. abortus* and *B. suis* endo-antigens are prepared by grinding or by means of ultrasonic waves, then by centrifugation. Glucidic-lipidic-polypeptidic antigens are prepared by means of trichloracetic acid. Non saturated anti-*melitensis*, anti-*abortus* and anti-*suis* sera have been used.

"The diffusion techniques used are the double diffusion method in Petri dish (Ouchterlony) and the slide micro-diffusion method (Scheidegger).

"The study of the precipitation lines shows that:

"1. Antigens extracted by grinding or by ultrasonics are quite identical.

"2. *B. melitensis*, *B. abortus* and *B. suis* endo-antigens are identical: they constitute the antigenic fraction common to all species of the *Brucella* genus.

"3. Glucidic-lipidic-polypeptidic antigens differ from the above antigens; they do not possess any common fraction with them.

"*Melitensis* and *abortus* GLP antigens are identical. *Suis* antigen is different and allows to distinguish the *suis* antigenic type from the *abortus* antigenic type."

HOLLAND, J. J. & PICKETT, M. J. **A Cellular Basis of Immunity in Experimental *Brucella* Infection.** *J. Exper. Med.* 1958, Sept. 1, v. 108, No. 3, 343–60, 6 charts & 6 figs. on 4 pls. [23 refs.]

In an ingeniously contrived tissue culture system in which peritoneal monocytes derived from normal rats, mice and guineapigs were used, intracellular multiplication of *Brucella suis, abortus* and *melitensis* was demonstrated. During the 3 days following infection complete engorgement of many monocytes in the cultures occurred although very few showed toxic effects. The rate of multiplication was diminished in monocytes derived from animals which had previously been immunized with cultures of smooth brucellae. Rough brucellae were shown to multiply at a slower rate in monocytes from normal animals and their rate of growth was considerably depressed in monocytes from animals which had previously been immunized with smooth organisms. The addition of *Brucella* antiserum to the culture medium did not affect the growth of smooth organisms in either normal monocytes or in cells derived from immunized animals. Desensitization of immunized guineapigs did not alter the refractory state of the monocytes. No cellular resistance was demonstrable in animals immunized with either heat-killed brucellae, despite the development of agglutinating antibody, or with living rough *Br. suis*.

[See also this *Bulletin*, 1957, v. 32, 376, 807.]

R. G. Sommerville

VAN DRIMMELEN, G. C. & STEYN, H. S. **The Keeping Quality of Freeze-Dried *Brucella abortus* Strain 19 Vaccine.** *J. General Microbiol.* 1958, Oct., v. 19, No. 2, 324–9, 2 figs.

The vaccine used in this work consisted of *Brucella abortus* S19, concentrated by sedimentation with sodium carboxymethylcellulose, freeze-dried in 4 ml. amounts in 10 ml. ampoules, with an anti-oxidant (ascorbic acid and thiourea). When this vaccine is sealed in nitrogen its loss of viability can be expressed as a coefficient whose value may be derived from the formula of a straight line fitting the means of the logarithms of the viability counts made 1 week to 6 months after freeze-drying. Knowing this coefficient would make it possible to predict the viable count of vaccine stored at 4°C. at distribution centres, which could be labelled in advance as regards dosage for several months after it had left the place of manufacture. Excess anti-oxidant and insufficient anti-oxidant both adversely affected the viability of the vaccine in storage, and for maximum stability the incorporated anti-oxidant should be balanced with the concentration of viable organisms present.

E. Agius

GARY, N. D., KUPFERBERG, L. L. & GRAF, L. H. **Characterization of Intracellular, Glucosidic Polysaccharide produced by *Brucella suis*.** *J Bacteriology*. 1958, Oct., v. 76, No. 4, 359–64, 2 figs. [18 refs.]

PARNAS, J., BEDNARSKI, S., KOZAK, R. & GALINSKI, J. Résultats de recherches concernant la sensibilité des souches de *Brucella* de notre collection à l'influence des antibiotiques. [**Results of Studies of the Sensitivity of Strains of *Brucella* in our Collection to antibiotics**] *Rev. d'Immunologie*. 1957, Oct.–Dec., v. 12, Nos. 5/6, 356–62, 2 figs.

These authors from Lublin give the results of various tests of the sensitivity of 190 strains of *Brucella* to oxy- and chlortetracycline, chloramphenicol and streptomycin. Apparently these strains included all 3 principal species, but separate findings for each species are not stated, or the total number of each examined. The paper consists largely of tables and graphs presenting the results with little information about how they were obtained; a method using discs is described, but there is no description of the method used in falling dilution tube tests of both bacteriostatic and bactericidal action the findings in which occupy 2 pages of tables. Some observations on "destruction" of the antibiotic in fluid cultures incubated for 3 days are referred to for the first time in a summary on the last page, and it is remarkable that the least stable of the 4 antibiotics, chlortetracycline, showed the lowest degree of loss of activity (8·7%, that of streptomycin being 87%). Some studies of combined action were also made with results favourable to the combination of chlortetracycline and streptomycin.

L. P. Garrod

MORRIS, E. J. **Selective Media for some *Pasteurella* Species.** *J. General Microbiol.* 1958, Oct., v. 19, No. 2, 305–11.

The 3 media which were of the greatest use were tryptic digest of beef agar (TMA) (for growth of *Pasteurella septica* and *P. pseudotuberculosis*), or Difco tryptose agar (TA) (for *P. pestis* and *P. haemolytica*) containing 5% (v/v) peptic sheep's blood (PSB), with the following additions:—

Medium 1. For *P. pestis* and *P. pseudotuberculosis*.
Novobiocin 10 μgm./ml. + potassium tellurite 5 μgm./ml. + erythromycin 5 μgm./ml. + Actidione 100 μgm./ml. *P. pseudotuberculosis* also grew on this medium when PSB was omitted.

Medium 2. For *P. septica*.
Neomycin 2·5 μgm./ml. + potassium tellurite 2·5 μgm./ml. + tyrothricin 10 μgm./ml. + Actidione 100 μgm./ml.

Medium 5. For *P. haemolytica*.
Neomycin 1·5 μgm./ml. + novobiocin 2 μgm./ml. + Actidione 100 μgm./ml.

These media were investigated for the isolation of the organisms from material heavily contaminated with other bacteria.

Charles Wilcocks

WESSMAN, G. E., MILLER, Donna J. & SURGALLA, M. J. **Toxic Effect of Glucose on Virulent** *Pasteurella pestis* **in Chemically Defined Media.** *J. Bacteriology.* 1958, Oct., v. 76, No. 4, 368–75, 4 figs. [12 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin,* 1959, v. 56, 154.]

KLEINMAIER, H. Die O-Gruppenbestimmung von *Pseudomonas*-Stämmen mittels Objektträger-Agglutination. [**O-Group Determination of** *Pseudomonas* **Strains by means of Slide-Agglutination**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 170, No. 8, 570–83. [10 refs.]

The author finds that the difficulty which has been experienced by most investigators in serological grouping of *Pseudomonas* strains by their O antigen content can be very simply overcome if the O sera are used on suspensions of living and untreated bacteria in slide agglutination tests. In this way the degradation of the bacterial antigen which arises in preparing O suspensions from *Pseudomonas* strains and makes them unsuitable for observations on agglutination, a point emphasized by MAYR-HARTING, is obviated.

The O sera used have been mainly those of HABS, in whose laboratory Kleinmaier works, but beyond the indication that the bacteria are subjected to steam, there is no detail given about the preparation of those sera. Hab's contribution on the subject is quoted as in the press.

Hab's differentiation of 12 O groups is confirmed, but some slight cross-agglutinations are observed which he overlooked but which can be eliminated if highly concentrated serum dilutions are not used. For the groups 2, 5, 7 and 8 the use of absorbed sera is recommended, however. The serum should give at least a titre of 1/200 when tested in the water bath and 1/80 when tested by the slide suspension method and should not be used in higher concentration than 1/10.

A useful point is that the most even suspensions of *Pseudomonas* strains for agglutination are obtained from cultures on MacConkey bile salt agar and that it is the bile salt which is apparently the important factor.

J. W. McLeod

COLLING, Margaret; NIGG, Clara; HECKLY, R. J. **Toxins of** *Pseudomonas pseudomallei.* **I. Production** *in vitro* [COLLING, NIGG & HECKLY]. *J. Bacteriology.* 1958, Oct., v. 76, No. 4, 422–6. [10 refs.] **II. Characterization** [HECKLY & NIGG]. *Ibid.,* 427–36, 5 figs.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin,* 1959, v. 56, 227.]

SARKAR, J. K. **Survival of** *V. cholerae* **and other Intestinal Pathogens in Water.** *J. Indian Med. Ass.* 1958, Aug. 16, v. 31, No. 4, 154–6.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin,* 1959, v. 56, 157.]

FARKAS-HIMSLEY, Hannah. **Metabolic Studies of Streptomycin Sensitive, Resistant and Dependent** *Vibrio comma* **(type Ogawa).** *Bull. Res. Counc. of Israel.* 1957, Dec., v. 6E, No. 3, 8. [10 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin,* 1959, v. 56, 158.]

FELSENFELD, O. & WATANABE, U. Y. **An Alkaline Tellurite Lauryl Sulfate-Salt Plate for the Isolation of** *Vibrio comma. U.S. Armed Forces Med. J.* 1958, July, v. 9, No. 7, 975–82. [10 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin,* 1959, v. 56, 157.]

WATANABE, Y. **Phage absorbed on Paper Disks in the Rapid Identification of** *Vibrio comma. Amer. J. Trop. Med. & Hyg.* 1958, May, v. 7, No. 3, 312–14, 1 fig.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin,* 1959, v. 56, 158.]

KOVTUNOVICH, L. G. **A New Method of detecting** *Clostridium botulinum* **Toxin.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1957, v. 28, Nos. 7/8, 1157–63. [Translated from Russian.]

MINERVIN *et al.* (*Zhurnal Mikrobiologii, Epidemiologii i Immunobiologii,* 1955, v. 5, 48; 1956, v. 6, 44) noted that *Cl. botulinum* toxin markedly inhibits the phagocytic activity of leucocytes both *in vivo* and *in vitro.* The effect is neutralized by specific antitoxic serum. They suggested that the changes in the phagocytic index to staphylococci in the presence of *Cl. botulinum* toxin should be utilized for the rapid detection of the toxin in the blood of human patients or animals and in food products, and also developed the technique of this reaction. In view of the great practical importance of this a series of experiments were undertaken to verify it experimentally.

Four series of experiments were carried out and moreover the method was tested on 2 cases of suspected botulism which occurred during the course of the experiments.

The first series of experiments aimed at verifying the possibility of utilizing the phagocytic index for the detection of pure botulinum toxin. Results showed that there was a close relation between the concentration of toxin, the mortality and the phagocytic index in that a reduction in the concentration of toxin regularly brought about an increase in the phagocytic index. Toxin doses which caused the death of all mice in the experiment gave low phagocytic indices; conversely doses which did not cause the death of all the mice in the experiment gave higher phagocytic indices approximately the same as those given by the control. It may be assumed that the method of detection of toxin by means of the phagocytic index is more sensitive than tests on mice.

The second series tested the specificity of the phagocytic reaction and showed that the addition of specific homologous antiserum caused complete neutralization of the toxin and stimulation of phagocytosis. Even a

very small amount of serum produced a neutralizing effect.

The feasibility and rapidity of detection of *Cl. botulinum* toxin in the blood of animals was investigated in the third experiment. Results showed that the phagocytic indices varied with the dose of toxin and the length of time which elapsed after inoculation. During the first 2 hours after subcutaneous injection of the toxin there was a stimulation of phagocytosis, especially after inoculation with doses which subsequently caused death of the mice. However, 4 hours after inoculation there was marked inhibition of phagocytosis, particularly in animals which died from intoxication. Some inhibition of the phagocytic index was also observed in animals which survived the injection of toxin, but after the second 24-hour period they returned to the original level. These results led to the conclusion that the phagocytic reaction permits the detection of *Cl. botulinum* toxin in the blood of artificially inoculated animals and the determination of its type. It must be remembered, however, that during the first 2 hours after the subcutaneous injection of the toxin a stimulation and not an inhibition of phagocytosis occurs.

The fourth series of experiments was carried out on food products artificially infected with toxin. Results showed that the phagocytic indices were inconclusive and gave no grounds for assumptions about the presence of toxins in the food. Specific neutralization tests were therefore carried out with type A and B antisera, and the results clearly showed that the homologous serum (type A) neutralized the toxin and stimulated phagocytosis while the heterologous antiserum (type B) produced no change in the index. The conclusion is drawn that the presence and type of *Cl. botulinum* toxin in a food product may be determined from phagocytic indices in the presence of specific type antiserum.

Finally, the results of testing sera from 2 patients with suspected botulism are described. A test in mice with these sera disclosed *Cl. botulinum* toxin of type A, but simultaneous tests by the phagocytic indices failed to give any information. Further blood samples were taken despite the fact that 48 hours had already elapsed and both patients had been given antiserum. These samples were tested by the method of Minervin and the phagocytic indices calculated. Results showed that, in the presence of specific homologous antiserum, the phagocytic index gave clear-cut results which showed the presence and type of *Cl. botulinum* toxin in the patient's blood even after inoculation with specific antiserum.

The final conclusion is that the phagocytic index, as determined by the method of Minervin *et al.*, enables small amounts of toxin to be detected in the blood of patients suffering from botulism, in artificially infected animals and in artificially infected foodstuffs and its type to be defined. This method is characterized by its rapidity, high sensitivity and specificity although the results do not always agree even when the experimental conditions are strictly observed. Thus, until a large amount of clinical and experimental results are available, tests in white mice must still be carried out in parallel. *P. A. Clearkin*

ORLANS, E. S. & JONES, V. E. **Studies on some Soluble Antigens of *Clostridium welchii* Types B, C and D.** *Immunology.* Oxford. 1958, July, v. 1, No. 3, 268–90, 26 figs. [27 refs.]

The general object of this investigation was to determine the degree of correlation which could be demonstrated between the findings with regard to toxin production by B, C and D types of *Cl. welchii* by the established methods of titration of these toxins, haemolytic action, neutralization by antitoxins etc. on the one hand and, on the other, by the lines of precipitation which they produced in gel diffusion observations based on Ouchterlony's method and modifications of it.

The paper contains a great deal of elaborate and careful work for which reference must be made to it. The general conclusions reached are that, although the principal toxic elements in filtrates of B and C strains, *i.e.* β and ϵ toxins in B filtrates and β toxin in C filtrates, could be satisfactorily demonstrated in the gel diffusion plates, these were not readily elicited unless a concentrated preparation of antigen was used. It was pointed out that where filtrates concentrated by ammonium sulphate precipitation and drying are used, quantitative errors are likely to arise and that identification of all the antigens which have been described for B and C strains has not been obtained on the one hand and, on the other, lines have appeared which seem to indicate antigens not yet recognized by other methods. The correlation of the data with regard to the toxin production by D strains already established and the development of lines in the gel diffusion plates, however, is good. The augmentation of ϵ toxin by tryptic digestion, *i.e.* its development from a non-toxic precursor was very convincingly demonstrated.

The strains used have been obtained from various collections and were found to contain 1 or 2 which did not strictly correspond to the accepted criteria of classification, *e.g.* there were 2 strains of C type which were found to yield ϵ as well as β toxin.

It was found that rabbit's blood was best for demonstration of α toxin, horse blood for θ, and sheep's blood for δ toxin. Of the C strains tested, all produced α toxin acting on rabbit's blood, 4 produced much, 4 moderate and 3 no δ haemolysin. The outstanding feature of some strains producing δ haemolysin was the completeness of the haemolysis and the potency, haemolytic activity being observed even up to a dilution of 1 : 20,000. *J. W. McLeod*

BERGER, U. Die Empfindlichkeit einiger sporenfreier Anaerobier gegen Spiramycin *in vitro*. [**The Sensitivity of some Non-Sporogenous Anaerobes to Spiramycin** *in vitro*] *Ztschr. f. Hyg. u. Infektionskr.* 1958, v. 145, No. 2, 160–65. [22 refs.]

The facts reported in this paper are that 6 strains of *Treponema microdentium*, the Reiter strain of *Trep. pallidum*, and 1 of *Borrelia vincenti* were inhibited by 0·1–0·5 μgm. per ml. of spiramycin, while 10 strains of *Fusobacterium* spp., unidentified, were uninhibited by 100 μgm. per ml. These findings are similar to those reported by the author in previous papers for other antibiotics of this group. [The writer of this abstract

(this *Bulletin*, 1956, v. 31, 677) found some strains of *Fusobacterium vincenti* (*Bacteroides fusiformis*) and of 3 other related organisms to be inhibited by much lower concentrations of erythromycin than this. It would be a mistake to regard the Gram-negative non-sporing anaerobes as in general highly resistant to antibiotics of this group.] *L. P. Garrod*

RICKETTSIAE

ROGER, F. & ROGER, A. Une variante simple d'emploi du colorant de Wright utilisable avec les rickettsies et les virus de groupe Trachome-Psittacose-Lymphogranulomatose. [**A Simple Modification of the Use of Wright's Stain for Staining Rickettsiae and Viruses of the Trachoma-Psittacosis-Lymphogranuloma Group**] *Bull. Soc. Path. Exot.* 1958, May–June, v. 51, No. 3, 307–9.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 141.]

GIROUD, P., LE GAC, P. & DUMAS, Nicole. La conservation à basse température n'a pas modifié le comportement de la souche de typhus épidémique isolée du sang de caprins en Éthiopie. [**Strain of Epidemic Typhus Isolated from a Goat in Ethiopia Unmodified by Preservation at Low Temperature**] *Bull. Soc. Path. Exot.* 1958, May–June, v. 51, No. 3, 304–6.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 142.]

SILICH, V. A. **The Survival of *Rickettsia burneti* in Infected Meat in Storage Conditions.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1957, v. 28, Nos. 5/6, 816–18. [12 refs.] [Translated from Russian.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 147.]

BACTERIOPHAGES

DEERING, R. A. & CHRISTIAN, Edith. **Action of T2 Bacteriophage on Filamentous** *Escherichia coli*. *Virology*. New York. 1958, Aug., v. 6, No. 1, 150–56, 3 figs.

E. coli B cells which have been irradiated with low doses of UV light continue to grow but do not divide, so forming long filaments. The filaments contain the same amount of nucleic acid per unit mass as normal cells, and therefore an increased amount per cell with greater length. The burst size of *E. coli* filaments infected with T2 was found to depend upon the cell length, but burst size did not increase as fast as cell volume, suggesting that something other than bacterial mass limited the number of phage particles produced. There was also a slight increase in latent period with length of cell, but not enough to account for the larger burst size. *Janice Taverne*

MAIO, J. J. & ZAHLER, S. A. **Observations on the Host-Induced Modification of T2 Bacteriophage with Special Reference to the Effects of α-Keto Acids.** *J. Bacteriology*. 1958, Sept., v. 76, No. 3, 256–63, 3 figs. [12 refs.]

T2 phage grown in some *Escherichia coli* B mutants undergoes host-induced modification and no longer multiplies in its original host. The modified phage T*2, still infects *Shigella dysenteriae* Sh to produce normal T2 progeny [this *Bulletin*, 1953, v. 28, 853]. However, about 1 in 1,000 *E. coli* B cells support the growth of the modified phage, yielding unmodified T2. When *E. coli* B is irradiated with UV light before infection, or grown in acid conditions or allowed to age, the number releasing phage increases to 50%.

The authors report that all *E. coli* B cells infected with the modified phage produced phage when irradiated with UV before infection if an α-keto acid, such as pyruvic, α-keto-glutaric or oxalacetic acid was present in the plating medium. The α-keto acids did not affect the viability of irradiated cells, but unless they were added up to 20 minutes after infection, all the infected cells did not produce phage. Phage, therefore, developed through some early stages before reaching a step for which an α-keto acid was required to ensure that the cell yielded mature phage. Amino-acids (including those corresponding to the α-keto acids), purines, pyrimidines and vitamins did not increase the number of phage-producing cells.

Whether or not *E. coli* B cells support the growth of the modified phage thus depends on physiological as well as genetic conditions. Irradiated cells exposed to pyruvate and washed before infection with the modified phage did not yield T2 unless pyruvate was present in the plating medium. The environment of the irradiated cells after infection therefore appears critical. It is not known why this is so. *Janice Taverne*

EDGAR, R. S. & STEINBERG, C. M. **On the Origin of High Negative Interference over Short Segments of the Genetic Structure of Bacteriophage T4.** *Virology*. New York. 1958, Aug., v. 6, No. 1, 115–28, 5 figs. [10 refs.]

The analysis of recombination involving closely linked genetic markers has shown that those T4 phage recombinants which result from more than one gene exchange appear in far greater number than would be predicted on the basis that exchanges in neighbouring regions are independent. This phenomenon is called "high negative interference". In theory, it could follow either several rounds of mating, or a single mating in which more than one exchange occurred. Experimentally, high negative interference was observed in crosses between 2 parent T4 strains with 3 different

closely linked markers in the r II region. Recombination values were measured in a series of crosses in which the relative frequencies of the 2 parents were systematically varied. It was concluded that most double recombinants resulted from a double exchange in a single mating event.

In crosses between 3 parents, progeny containing markers from each of the 3 can only arise, theoretically, as a result of at least 2 exchanges occurring in 2 different matings. Experimentally, negative interference between closely linked markers was again observed in crosses between 3 parents. It occurred, however, to a lesser extent, and arose during the course of multiple matings. *Janice Taverne*

LANNI, F. **Immunogenetic Dissection of the T5 Bacteriophage Tail.** *Science.* 1958, Oct. 10, v. 128, 839–40.

NORTHROP, J. H., with the technical assistance of Marie KING. **Studies on the Origin of Bacterial Viruses. I. The Incidence of Phage-Producing Cells in Various *B. megatherium* Cultures. II. The Effect of Ultraviolet Light on the Incidence of Phage-Producing Cells and of Terramycin-Resistant Cells. III. The Effect of Hydrogen Peroxide on the Incidence of Phage-Producing Cells and of Terramycin-Resistant Cells. IV. Calculation of the Incidence of Phage-Producing Cells.** *J. General Physiol.* 1958, Sept. 20, v. 42, No. 1, 109–36, 9 figs. [Numerous refs.]

KELLER, R. **Passage of Bacteriophage Particles through Intact Skin of Mice.** *Science.* 1958, Sept. 26, v. 128, 718–19, 1 fig. [10 refs.]

A bacteriophage derived from *Bacillus megatherium* could be recovered from the blood of mice up to 2 hours after the phage suspension had been applied to the intact skin, either on the abdomen or tail. The skin was not depilated and the mice were isolated before the experiment, to reduce skin damage. A large number of mice were tested and the recovery of active phage was irregular. This irregularity and the rapid disappearance of phage may be caused by natural antibodies or the properdin system or both: properdin has been shown to inactivate T2 phage and a *Staphylococcus* phage. The head of the *B. megatherium* phage is 49 mμ wide and of the same order of size as some animal viruses. The author hopes that his report will make workers consider the possibility that the passage of virus through intact skin could lead to infection.
Janice Taverne

VIRUSES

In this section the abstracts are arranged as far as possible in the following order: General; Psittacosis-lymphogranuloma viruses; Pox viruses; Respiratory and other viruses; Enteric viruses; Arthropod-borne viruses; Others.

ORFILA, Jeanne. Sensibilité à différents virus des cultures des cellules rénales de souris. **[Sensitivity of Murine Kidney Cell Cultures to Different Viruses]** *C.R. Soc. Biol.* 1958, v. 152, No. 2, 342–3.

The author describes the use of monolayer cultures prepared from murine kidney for the study of viruses. The following viruses were found to produce cytopathic effects in such murine kidney cultures: Coxsackie B 1–5, adenovirus 1–7, herpes simplex and measles viruses. On the other hand, poliovirus Types 1, 2 and 3, ECHO 9 and mumps viruses did not produce cytopathic effects. Experiments establishing that any of these viruses could be propagated in murine kidney cells are not described. The author speculated whether murine kidney cells from pure lines of mice would be of uniform sensitivity to viruses, and also whether "foamy" and other viral agents that have been found to be such a problem with monkey kidney cells will also prove to be troublesome in these cells as more experience is obtained. *A. J. Beale*

MALHERBE, H. & HARWIN, R. **Neurotropic Virus in African Monkeys.** [Correspondence.] *Lancet.* 1958, Sept. 6, 530.

African monkeys are being used increasingly for tissue culture methods, so that there is special importance in this letter from the Poliomyelitis Research Foundation Laboratories of the South African Institute for Medical Research in Johannesburg. On 2 occasions the authors have isolated a virus resembling the B virus of SABIN and WRIGHT [this *Bulletin*, 1934, v. 9, 427] from the central nervous system tissues of the African vervet monkey *Ceropithecus aethiops pygerythrus*. Nuclear inclusions and small syncytiae were found in cultures of monkey-kidney epithelium. In rabbits inoculated intradermally and subcutaneously necrosis of the skin occurred: in some cases paralysis and death resulted and the virus was isolated from brain and spinal cord of paralysed animals.

Neutralization tests with anti-B virus showed a serological relationship between B virus and the new agent, which the authors designate SA8 in their series [*ibid.*, 1958, v. 33, 187]. *H. J. O'D. Burke-Gaffney*

HAMPARIAN, V. V., MÜLLER, F. & HUMMELER, K. **Elimination of Nonspecific Components from Viral Antigens by Fluorocarbon.** *J. Immunology.* 1958, June, v. 80, No. 6, 468–75.

The authors have previously reported [this *Bulletin*, 1957, v. 32, 1205] the use of Freon 112 (1 : 2-difluorotetrachlorethane) in the preparation of poliomyelitis complement-fixing antigens free from host components, and in the present work the method has been extended

and applied to Coxsackie, ECHO and other antigens as well. Crude antigens consisting of mixed HeLa cell débris and culture fluid infected with the 3 types of poliomyelitis virus, Coxsackie A type 9 and B type 1, adenovirus type 6, ECHO type 6 or influenza A (PR8), saline extracts of chorio-allantoic membranes infected with mumps or PR8 viruses, and extracts of infant mouse carcass infected with Coxsackie A type 4 virus were homogenized with one-half volume of Freon 112 dissolved in *n*-heptane to make a solution of specific gravity 1·30. After centrifugation a sample of the aqueous phase was removed for testing and the fluorocarbon treatment was repeated on the remainder. The treatment abolished the anticomplementary activity of the crude antigens, in most cases without affecting specific antigenic activity, and also removed antigens fixing complement with guineapig antisera to host proteins. The V and S antigens of influenza and mumps were affected by the treatment and were completely removed by 2 exposures to the fluorocarbon.

D. J. Bauer

CHARDONNET, Y. Étude de l'immunité expérimentale du cobaye contre le virus des oreillons. I. Recherche des facteurs influençant la production d'anticorps fixant le complément après immunisation primaire. [**Experimental Immunity to Mumps in Guineapigs. I. Factors Influencing the Production of Complement-Fixing Antibodies after Primary Immunization**] *Rev. d'Immunologie.* 1958, Apr.–June, v. 22, No. 3, 166–90. II. Recherches sur les modalités d'apparition des anticorps fixant le complément après immunisation secondaire (phénomène de rappel). [**II. Complement-Fixing Antibody Response after Booster Doses**] *Ibid.*, 191–221.

I. Some of the factors affecting the production of mumps complement-fixing antibodies in guineapigs were investigated. Antibody production was stimulated by 5 different virus strains administered by the intranasal, intradermal, intraperitoneal and intracardiac routes. A comparison of complement-fixing titres following virus administration by different routes revealed a more rapid antibody production after intranasal inoculations where maximal titres were reached between 12 and 14 days. Allantoic or amniotic fluids with a haemagglutination titre of 1/160 stimulated antibody production when inoculated at 10^{-3} but not at 10^{-4} dilutions. Storage of virus materials at −20°C. caused a reduction in antigenicity. Persistence of antibody for periods up to 370 days was demonstrated. The method of "concentrated immunization", consisting of repeated inoculations at the same site, did not result in increased responses.

II. The antibody response of immune guineapigs to booster doses of mumps virus was investigated. Primary and secondary responses could be obtained following the inoculation of virus containing egg fluids or pathological materials such as saliva or cerebrospinal fluid. The magnitude of primary and secondary responses was often correlated. A rise in complement-fixing antibody occurred usually 4–12 days after the booster dose. Several routes of inoculation were used for primary and secondary immunization. Secondary responses were approximately identical with several different strains of mumps virus, suggesting the existence of a single antigenic virus type. Specificity of the antibody response was demonstrated in animals primarily immunized both with influenza and mumps virus and subsequently inoculated with each of the 2 viruses. A cerebrospinal fluid from a patient with mumps, and from which no virus could be isolated by egg inoculation, gave rise to booster responses when inoculated to mumps-immune guineapigs.

H. G. Pereira

STOKER, M. G. P., SMITH, K. M. & ROSS, R. W. **Electron Microscope Studies of HeLa Cells infected with Herpes Virus.** *J. General Microbiol.* 1958, Oct., v. 19, No. 2, 244–9, 10 figs. on 7 pls. & 1 text fig.

The multiplication of herpes simplex virus in the HeLa cells was studied by infectivity titrations and by electron microscopy in cultures inoculated with large virus doses and examined after varying times of incubation. In spite of the large virus inocula employed, only 6% of the cells could be shown to yield virus when inoculated on chick embryo chorio-allantoic membranes. The first increase of virus infectivity occurred in the cellular fraction of the cultures between 9 and 12 hours' incubation and high infective titres were reached at 26 hours, both in the cellular and fluid fractions. Virus particles were first seen by electron microscopy in the nuclei of 2 of 25 cells examined at 12 hours. At 26 hours many cells contained virus particles with a central dense granule surrounded by a single membrane in intranuclear virus and a double membrane in particles situated in the cytoplasm or on the cell surface. In cultures inoculated with smaller virus doses and examined after 96 hours' incubation, virus particles were seen in many cells, mostly in the nuclei and on the cell surface. The nuclei from infected cells showed loss of granular material, except at the nuclear margin. *H. G. Pereira*

STOKER, M. G. P. & ROSS, R. W. **Quantitative Studies on the Growth of Herpes Virus in HeLa Cells.** *J. General Microbiol.* 1958, Oct., v. 19, No. 2, 250–66, 6 figs. [15 refs.]

This is a detailed study of the growth of herpes simplex virus in HeLa cells. Cultures containing known numbers of cells were inoculated with large virus doses in an attempt to ensure a single cycle of virus multiplication. Virus adsorption, multiplication and release were investigated by means of pock titrations in chick embryo chorio-allantoic membranes. It was preliminarily found that 10 or more pock-forming units were required to initiate infection in HeLa cells. A high proportion of pock-forming units could, however, be adsorbed on to HeLa cells. The greater part of this adsorbed virus was superficially attached to the cells and could be neutralized by antiserum. A small fraction, in addition, resisted antiserum treatment, but could be liberated from the cells by treatment with ethylene diamine tetra-acetic acid (EDTA)

and probably corresponds to virus particles trapped in invaginations of the cell surface. Estimations of the number of virus-yielding cells were attempted by inoculation of cell suspensions on to chick embryo chorio-allantoic membranes, and the values obtained were lower than expected from the calculated multiplicities of infection. Possible reasons for this result are discussed in detail. During the latent period, virus could only be detected in a small minority of cells which eventually release virus, suggesting that virus multiplication is preceded by an eclipse phase. In cultures infected with more than 1 HeLa infectious unit per cell, new virus appears at 12 hours in the cell fraction and is released into the medium 4 hours later. *H. G. Pereira*

Ross, R. W. & Orlans, Eva. **The Redistribution of Nucleic Acid and the Appearance of Specific Antigen in HeLa Cells infected with Herpes Virus.** *J. Path. & Bact.* 1958, Oct., v. 76, No. 2, 393–402, 26 figs. (6 coloured) on 5 pls. [12 refs.]

"HeLa cells infected with herpes virus show a complete breakdown of particulate nuclear deoxyribonucleic acid (DNA) and a deposition of much diffuse DNA near the nuclear membrane.

"DNA appears before viral antigen can be detected; in successive stages more and more diffuse DNA becomes associated with viral antigen, suggesting that accumulation of diffuse DNA is a necessary step in the synthesis of viral antigen.

"These changes are associated with the formation of large giant-cells, probably formed by fusion and contraction of infected individual cells and, to a much less extent, by nuclear division in undivided cells. The early production of focal necrotic lesions in the presence of immune serum suggests that cell-to-cell spread may be due to a virus precursor rather than to fully formed virus."

Beswick, T. S. L. **Experimental Herpes Simplex Infection in the Baby Mouse.** *J. Path. & Bact.* 1958, July, v. 76, No. 1, 133–42, 13 figs. (11 on 3 pls.).

A study has been made of the pathology of herpes infection in infant mice. The egg-adapted GOS/CA reference strain inoculated intraperitoneally produced subcapsular necrosis of the liver and lesions in other abdominal organs, but did not affect the central nervous system. Another strain (F) produced myelitis without any involvement of the liver, but lost its affinity for the central nervous system during the course of passage in infant mice and acquired the ability to produce lesions in the liver and abdominal organs. A similar change in properties was observed when the F strain was passaged on the chorio-allantoic membrane and rabbit cornea. *D. J. Bauer*

Takátsy, G., Barb, K. & Farkas, E. **The Antigenic Structure of the Influenza Virus Strains isolated in Hungary in 1957.** *Acta Microbiologica.* Budapest. 1958, v. 5, No. 3, 287–96, 1 fig. [12 refs.]

Antigenic relationships between influenza virus strains isolated during 2 separate epidemics observed in Hungary in 1957 were studied by haemagglutination-inhibition, cross-antibody absorption and serum-neutralization tests. The first epidemic occurred in February and March, mainly among children under 4 years of age. Virus strains isolated during this epidemic showed a close antigenic relationship with A-prime strains prevalent at the immediately preceding widespread epidemic in Hungary. Evidence suggesting a progressive antigenic variation of A-prime influenza viruses is presented. The second epidemic occurred during the autumn, and was caused by the Asian type of influenza virus. The virus strains isolated during this second epidemic showed, however, some antigenic difference from the Singapore 1/57 strain as revealed by cross-haemagglutination inhibition and cross-serum absorption tests. The Hungarian strains showed in addition a minor antigenic component shared with A-prime strains. The possibility of recombination between Asian and A-prime strains is considered. *H. G. Pereira*

Koch, A. & Csonka, E. **Effects of Formaldehyde on Influenza Virus. II. Effects on the Infectivity of the Virus.** *Acta Microbiologica.* Budapest. 1958, v. 5, No. 3, 311–16, 4 figs.

The inactivation of A-prime influenza virus by formaldehyde was studied under varying conditions of temperature, *p*H and formaldehyde concentration. Inactivation rates increased with increasing *p*H, temperature and formaldehyde concentration. Under conditions giving high inactivation rates the reaction appears to follow first-order kinetics, and the authors suggest that inactivation is the result of a reaction of addition between formaldehyde and amino groups, leading to an irreversible bond. Under less favourable conditions the inactivation curves are irregular and it is suggested that "reactivation" of infectivity may take place on dilution.

[For part I, see this *Bulletin*, 1958, v. 33, 190.]
H. G. Pereira

Nász, I., Tóth, M. & Lengyel, A. **Adenoviruses isolated from Excised Tonsils.** *Acta Microbiologica.* Budapest. 1958, v. 5, No. 3, 267–9. [14 refs.]

Three strains of adenovirus, identified by serum neutralization as type 2 (1 strain) and type 5 (2 strains), were isolated from 12 samples of human tonsil and adenoid tissues cultivated *in vitro*. *H. G. Pereira*

Reichelderfer, T. E., Chanock, R. M., Craighead, J. E., Huebner, R. J., Turner, H. C., James, W. & Ward, T. G. **Infection of Human Volunteers with Type 2 Hemadsorption Virus.** *Science.* 1958, Oct. 3, v. 128, 779–80.

Type 2 haemadsorption virus [this *Bulletin*, 1958, v. 33, 621] an agent recently described in association with respiratory illness in children and included in the myxovirus group, was administered to 32 volunteers

ranging in age from 21 to 46 years. The virus strain used was isolated from the throat swab of an infant with acute laryngotracheobronchitis. Fluid from first-passage monkey kidney cultures was administered undiluted, each volunteer receiving a total volume of 1 ml. (80 TDC50) by swabbing the posterior oropharynx and the lower palpebral conjunctivae, and by spraying and instillation into the nose and pharynx. Volunteers were kept in isolation for 5 days following inoculation. Evidence of infection of 25 volunteers was supplied by virus isolation and serological investigations. Of these 25 volunteers, 18 had neutralizing antibodies for type 2 haemadsorption virus in pre-inoculation serum samples. No clinical illness was observed during the period of isolation, but 18 volunteers developed respiratory illness shortly after. The most common symptoms were nasal obstruction and discharge, coughing and sneezing. Most patients recovered within 2–3 days. Laboratory evidence of infection by type 2 haemadsorption virus was obtained in all but 1 of the volunteers with clinical illness. An institutional outbreak of a "cold-like" illness associated with the same virus occurred 8 days after the premature release of the volunteers from isolation. *H. G. Pereira*

SHAVER, Dorothy N., BARRON, A. L. & KARZON, D. T. **Cytopathology of Human Enteric Viruses in Tissue Culture.** *Amer. J. Path.* 1958, Sept.–Oct., v. 34, No. 5, 943–63, 7 figs. on 2 pls. & 3 text figs. [22 refs.]

The authors have studied the cytological changes produced by human enteroviruses (poliovirus, Coxsackie and ECHO) in monkey kidney cultures. The changes for Type 1 poliovirus are described in detail. These followed essentially descriptions given by previous workers. Large eosinophilic granules appeared in the nuclei early in infection (4 hours) and disappeared as the nucleus became pyknotic and shrunken. A large eosinophilic cytoplasmic mass appeared after about 4 hours and increased in size to occupy the whole cytoplasm. About 6 hours after infection vacuoles and protrusions occurred at the periphery of the cell and finally the cell became rounded and shrunken. Essentially similar changes were seen with Coxsackie and ECHO viruses (except ECHO 10) but the changes progressed more slowly except for ECHO 7 and 9 viruses.

ECHO 10 which differs from the other ECHO viruses [this *Bulletin*, 1956, v. 31, 872] produced characteristic cellular changes. Many cells contained homogeneous deeply eosinophilic irregular masses in the cytoplasm. Sometimes these masses were divided into globules or spread as thin strands. Scattered throughout the culture cells resembling keratinized squamous cells were seen. Uninfected cells maintained under normal and various adverse conditions rarely produced changes likely to be confused with the changes induced by the viruses. Small eosinophilic intranuclear granules were often seen, but these were much smaller and stained more weakly than those seen in infected cultures. Eosinophilic cytoplasmic areas were also seen in some degenerating cells. In a degenerating culture dying cells were often engulfed in the cytoplasm of other cells as eosinophilic masses. [The eosinophilic masses shown by cells infected with ECHO 10 virus have also been seen by the abstracter in cells infected with Croup Associated viruses.]

A. J. Beale

ALEXANDER, Hattie E., KOCH, G., MOUNTAIN, Isabel M. & VAN DAMME, Olga. **Infectivity of Ribonucleic Acid from Poliovirus in Human Cell Monolayers.** *J. Exper. Med.* 1958, Oct. 1, v. 108, No. 4, 493–506, 1 fig. [18 refs.]

Ribonucleic acid (RNA) prepared from concentrated and partially purified poliovirus of Types 1 and 2 by the method of GIERER and SCHRAMM (*Ztschr. f. Naturforsch*, 1956, v. 11, 138; *Nature*, 1956, v. 177, 702) was found to produce cytopathic effects and poliovirus of the type from which the RNA had been derived when added to monolayers of HeLa or human amnion cells. The infectivity was not due to residual complete virus but to the RNA because, (a) unlike complete virus it was inactivated by ribonuclease and normal serum (because of its RNase content); (b) unlike complete virus it was not inhibited by globulin from type-specific antiserum. The RNase used was crystalline and free from deoxyribonuclease. DNase in sufficient concentration to destroy the transforming principle of *Haemophilus influenzae* was without effect on the infectivity of the RNA from poliovirus. Similarly chymotrypsin and papain were without effect. Invasion of some cells takes place within 30 seconds of contact with the RNA, but the maximal effect was noted when the contact time was between 10 and 20 minutes. In these experiments undiluted RNA usually produced confluent or nearly confluent destruction of cell monolayers under agar, but no plaques on dilution. It has recently been discovered that by the use of appropriate diluents a linear relationship between dilution and number of plaques can be demonstrated. The poliovirus used for extraction of RNA is 0·88 M (with respect to NaCl) and after extraction with phenol 0·5 M. Dilution of this material in physiological salt solutions is associated with loss of infectivity, but infectivity is preserved in hypertonic solutions. The best diluent is thought to be 1 M NaCl buffered with 0·04 M sodium phosphate *p*H 7·2, but investigations are still in progress. *A. J. Beale*

BÁRDOS, V. **The Use of Suckling White Rats in the Virological Diagnosis of Tick-Borne Encephalitis and Equine Encepha'omyelitis.** *Acta Virologica.* Prague. 1957, July–Dec., v. 1, Nos. 3/4, 172–9. [19 refs.]

Wistar rats 3 days old were used. The strains of eastern and western equine encephalomyelitis virus used were obtained from Bratislava. Acetone-ether-extracted complement-fixing antigens were successfully made from rat brain for all 3 viruses. Hyperimmune serum was produced by inoculation of adults rats with infected suckling rat brain plus adjuvants. An intraperitoneal neutralization test for tick-borne encephalitis was found to be about as sensitive as a similar test in

adult mice. Intraperitoneal tests were also performed in suckling rats for the strains of eastern and western equine encephalomyelitis viruses. With these tests antibodies were found in wild and domestic animals to both eastern and western viruses and in human beings to eastern virus. [These results should be confirmed in another laboratory as their implications are of great importance.] *C. E. Gordon Smith*

BÁRDOS, V. **Natural Foci of the Western Type of North American Equine Encephalomyelitis (WEE) in Czechoslovakia. V. Isolation of the WEE Virus from the Brain of** *Apodemus flavicollis*. *Acta Virologica*. Prague. 1957, July–Dec., v. 1, Nos. 3/4, 198–202, 1 fig. [11 refs.]

Attempts were made to isolate viruses from the brains of wild rodents in the neighbourhood of the "city of B" (!) in the Danube Basin. 6 brains of *Apodemus flavicollis* were pooled as a 10% suspension and inoculated intracerebrally into 4 white mice (strain HA). One died and two were killed on day 3. The brains of the latter were blind-passed and the 4th mouse died on day 5. In the 2nd passage mice died on days 2, 3 and 4. In the 3rd passage the mice died after 48 hours. Re-isolation was not attempted because of technical difficulties. The virus was shown to be identical with a strain of western equine encephalomyelitis virus obtained from Bratislava, by cross-complement fixation, cross-neutralization tests, and cross challenge in mice.

[This is one of a number of reports of the occurrence of North American encephalomyelitis viruses in central Europe. These findings are of great importance if substantiated but it is highly desirable that they should be confirmed by work carried out in other laboratories especially those experienced in this group of viruses.] *C. E. Gordon Smith*

HAMMON, W. McD., SCHRACK, W. D., Jr. & SATHER, G. E. **Serological Survey for Arthropod-Borne Virus Infections in the Philippines.** *Amer J. Trop. Med. & Hyg.* 1958, May, v. 7, No. 3, 323–8, 1 fig. [13 refs.]

Sera were collected from (a) Negrito villagers living in the jungle, and (b) from Filipino schoolchildren and adults; both these groups were from near Clark Air Force Base, located about 60 miles North of Manila. Sera were also collected from Filipino children in Manila. Antibodies to Japanese encephalitis virus were commonest in the Negritos, less so in the nearby Filipinos, and least common in Manila. Dengue antibodies were common in all three groups. Other group B arborviruses used were: Uganda S against which no antibodies were found in 73 sera; Murray Valley encephalitis against which 60/215 had neutralizing antibody, 8 of them without associated Japanese encephalitis antibody; West Nile with 63/208 positive sera 11 of them without antibody to Japanese encephalitis virus; Ntaya with 65/177 positive sera was commonest in Manila, and 12 of these sera were negative to all the other B viruses used; Zika to which 19/153 sera were positive, 3 of them negative to all the others; St. Louis encephalitis to which 36/176 were positive but none without antibody to other B viruses; and Ilheus to which 16/163 were positive, none without related antibodies. No antibodies were found in human sera to eastern equine encephalomyelitis virus but 7 of 24 horses and 1 of 18 carabao were found positive [this virus was reported to have been isolated from a monkey in Manila, this *Bulletin*, 1949, v. 24, 914]. Western equine encephalomyelitis antibody was found only in 1 of 24 horses. Antibody to Semliki Forest virus was found in 18 of 119 human beings. No antibodies were found to Bunyamwera or Bwamba viruses.

The authors suggest that these results probably indicate the presence in the Philippines of Japanese encephalitis, dengue and eastern equine encephalomyelitis viruses at least 2 other members of group B (including a virus closely related to Ntaya), and a virus closely related to Semliki Forest virus.

C. E. Gordon Smith

HOTTA, T. **An Interference Diagnosis Method of Japanese Encephalitis Virus on Developing Egg and Tissue Culture of Chick Embryo.** *Med. J. Osaka Univ.* 1958, Mar., v. 8, No. 44, 675–84, 2 figs. [17 refs.]

This is a quantitative study in embryonated eggs of the interference by Japanese encephalitis virus with the multiplication of influenza and western equine encephalomyelitis viruses. Allantoic inoculation of eggs incubated more than 11 days to eliminate deaths due to Japanese encephalitis virus was mainly used. Haemagglutination was used to indicate growth of influenza virus and embryo death for indicating that of western equine virus. The titre of Japanese encephalitis virus determined by interference was approximately equal to its titre by infectivity titration. A lower dosage of ultra-violet irradiation destroyed the ability of the virus to interfere more than was necessary for destruction of its infectivity. Interference with western equine virus in chick embryo fragments in tissue culture was also demonstrated. Interference by Japanese encephalitis virus could be inhibited by antiserum to it. *C. E. Gordon Smith*

KUMA, N.; KONDO, A.; YOSHINO, K.; KITAOKA, M. **Infection of the One-day Old Fertile Hen's Egg with Rabies Virus. III. Some Observations on High Egg Passage (HEP) Strains** [KUMA]. *Japanese J. Med. Sci. & Biol.* 1958, Apr., v. 11, Nos. 1/2, 31–43, 1 fig. **IV. A Quantitative Analysis of Infective Units for Mice (MIU) and for One-Day Eggs (OIU)** [KONDO]. *Ibid.*, 45–57. [30 refs.] **V. Cultivation of Different Strains in the Egg-White-Replaced One-Day Egg (ERO) with special reference to interference between Adult-Mouse-Pathogenic and Non-Pathogenic Strains** [YOSHINO, KONDO, KUMA & KITAOKA]. *Ibid.*, 59–71, 2 figs. [23 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 151.]

PANTHIER, R. & HANNOUN, C. Examens microscopiques comparatifs de certaines altérations cellulaires d'origine virale (K.C.E.). Étude et discussion. **[Comparative Microscopical Examination of Cellular Changes due to the Virus of Keratoconjunctivitis]** *Bull. Soc. Path. Exot.* 1958, May–June, v. 51, No. 3, 366–73, 5 figs. on 2 pls. [17 refs.]

IMMUNITY

MAKINODAN, T. & GENGOZIAN, N. **Primary Antibody response to a Distantly Related Heterologous Antigen during Maximum Depression Period after Varying Doses of X Radiation.** *J. Immunology.* 1958, Aug., v. 81, No. 2, 150–54, 5 figs. [16 refs.]

In previous papers [this *Bulletin*, 1957, v. 32, 390; 1958, v. 33, 897] the authors have defined with precision a set of standard conditions for obtaining maximum agglutinin responses to sheep red blood cells in inbred $(C3H \times 101)F_1$ mice, and they have investigated successive aspects of the effect of X-irradiation on the immune response. The maximum depressant effect was observed when mice were irradiated 1 day before antigen injection. In the present paper, the effect of varying the X-ray dosage has been investigated.

The mean peak titre of antibody did not vary consistently with X-ray dosage. The other characteristics of immune response (induction period, rate of appearance of circulating antibody and total antibody produced) were all related to the dose of X-rays in curvilinear fashion. The maximum rate of change from the normal pattern occurred with exposures between 500 r and 800 r [the 30-day LD50 dose of X-rays was 756·3 r].

The administration of normal isologous bone-marrow to X-irradiated mice before antigen-injection increased the overall survival time and survival rate as would be expected. However, the induction period of immune response was no shorter in these animals than in those not given marrow. The authors conclude that no detectable amount of cells capable of antibody production are donated by this procedure.

Derek Hobson

GONCHARENKO, I. M. **The Influence of Ionizing Radiation on Antitetanus Antitoxic Immunity.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1957, v. 28, Nos. 7/8, 1012–17. [Translated from Russian.]

The majority of investigators consider that the exposure of animals to radiation before immunization has one of two consequences: either fewer antibodies are produced or else the process is retarded. Hitherto most of the studies have been concerned with formation of lysins, precipitins and agglutinins, but comparatively little has been done on the influence of radiation on antitoxic immunity.

The author was concerned with the effect of X-rays on the development of anti-tetanus antitoxic immunity and with the development of immunity in animals subject to radiation at various stages before, during and after immunization. The results showed that rabbits exposed to X-ray doses of 600–800 r and injected with crude tetanus toxoid at various stages after irradiation showed a decrease in the amount of antitoxin produced. These results do not disagree with those of other observers who investigated the formation of other varieties of antibodies after irradiation. A further series of experiments showed that after antibodies are formed they are not affected by irradiation. Experiments with guineapigs showed that the amount of antitoxin produced in the serum was determined by the nature of the antigen and the number of injections. The best results were obtained with 2 doses of adsorbed toxoid; 2 doses of a crude preparation produced a much smaller amount of antibody. Preliminary irradiation of guineapigs 7 days before immunization did not lead to complete inhibition of immunogenesis, which may be accounted for by the fact that some were inoculated with adsorbed antigen which creates a depot which persists for some length of time. Moreover, it has been found that antibodies may be formed in animals exposed to radiation by increasing the frequency of the antigen injections. A third group of guineapigs received their second injection of toxoid 27 days after exposure to radiation, but symptoms of local tetanus which did not appear in any of the other groups were present in this one.

Guineapigs exposed to radiation preserved to some extent balance between the concentration of antitoxin in the blood and the intensity of the active immunity.

P. A. Clearkin

FINGER, I. & KABAT, E. A. **A Comparison of Human Antisera to Purified Diphtheria Toxoid with Antisera to Other Purified Antigens by Quantitative Precipitin and Gel Diffusion Techniques.** *J. Exper. Med.* 1958, Oct. 1, v. 108, No. 4, 453–74, 5 figs. [49 refs.]

"The limits of sensitivity of three gel diffusion methods are compared and their utilization in the detection of small amounts of antibody to antigens present in traces in a preparation is illustrated with the diphtheria toxin-human antitoxin system. The Preer modification of the Oakley-Fulthorpe technique and the Oudin tube method were found more sensitive than the Ouchterlony plate method, and permitted the detection of as little as 3 μg. antibody N/ml. of serum.

"Antisera from eight Schick-negative individuals immunized with purified diphtheria toxoid have all been shown to contain, in addition to antitoxin, antibodies to substances present as impurities in the purified toxoid injected. The amounts of these antibodies in a serum and a partial characterization of their antigen-antibody curves have been determined through the combined use of quantitative precipitin and gel diffusion methods.

"Different amounts of antibody have been precipitated by toxin and toxoid from individual sera. Evidence is

presented that this may have been due to slight differences in antigenic specificity.

"A serum, Hu, which had been held to contain no precipitating antibody, has now been shown, by the Preer and Oudin techniques, to contain at least 12 μg. of precipitating antibody N (per ml. serum) against an impurity in the toxoid preparation. This estimate has been confirmed by quantitative precipitin determinations. The presence of antibodies to impurities in all human antitoxins examined in the present work brings into question the assumption that human antitoxin as such has a skin-sensitizing capacity."

COWAN, K. M. **Interpretation of Properdin Levels determined by Phage Neutralization Technique.** *Science.* 1958, Oct. 3, v. 128, 778–9. [11 refs.]

Normal serum, through its properdin system, has been shown to neutralize phage T2 (VAN VUNAKIS *et al.*, *Proc. Nat. Acad. Sci. U.S.*, 1956, v. 42, 391). It is reported here that different human sera neutralized phages T2, T6 and T7 to varying degrees. (No phage neutralization was observed with heated serum.) The ratio of the neutralization titres against the 3 phages was not constant for each serum tested, indicating that the differences observed did not reflect differences in phage susceptibility to one substance. It appeared instead that the neutralizing substance or substances had some specificity and varied in quantity from serum to serum. Measurement of properdin with T2, as has been proposed, would thus give a different answer from one obtained with another phage. Other workers have failed to find a correlation between properdin titres obtained with zymosan and either phage or tanned red cells.

The author concludes that either there must be several different properdins, or that properdin is a family of cross-reacting antibodies which can combine with zymosan. His work provides evidence for the theory that properdin may be natural antibody, but he emphasizes that if this is so, then our concepts of natural antigen-antibody reactions must be widened to include those cases in which complement is an essential co-factor, since the properdin system requires complement for its activity. *Janice Taverne*

NELSON, R. A., Jr. **An Alternative Mechanism for the Properdin System.** *J. Exper. Med.* 1958, Oct. 1, v. 108, No. 4, 515–35, 2 figs. [18 refs.]

"Evidence is presented that phenomena ascribed to the properdin system may be explained in terms of classical antibody (Ab) in combination with three of the components of complement (C'), *i.e.*, C'_1, C'_4, and C'_2 respectively. The results suggest that the complex of properdin (P) with zymosan (Z) represents a mixture of $Z{\cdot}Ab$, $Z{\cdot}Ab{\cdot}C'_{1,4}$, $Z{\cdot}Ab{\cdot}C_{1,4,2}$, and $Z{\cdot}Ab{\cdot}C'_{1,4,2}$ in a decayed state.

"The purported preferential reactivity of Z with the third component of C' (C'_3) is not supported by the present experiments in which Z was reacted with C' in both guinea pig and human sera. Approximately the same number of reactive units of $C'_{1,4}$ and of C'_3 were inactivated by Z, as well as by *D. pneumoniae* and a washed specific precipitate of bovine albumin–anti-albumin.

"The latter evidence that small amounts of antigen-antibody complex fix significant amounts of C'_3 stands in contrast with the classical concept that C'_3 is not fixed in ordinary complement fixation reaction. The observed reactivity of C'_3 is explained on the basis of the present use of essentially undiluted serum as a source of C'_3 and of 37° as the temperature for fixation.

"Ancillary data indicate that purified properdin contains Ab. In the presence of a chelating agent and at 0° properdin agglutinated Z granules. Measurements of nitrogen (N) uptake by Z suggest that 0.25 μg. N were contributed by solutions stated to contain 1 unit of properdin.

"The broad spectrum of reactivity or cross-reactivity of the Ab in normal serum is likely due to the wide distribution in nature of closely related polysaccharides. Further immunochemical studies are necessary to establish definitively the origin and mode of action in 'natural resistance' of antibodies reactive with these polysaccharides."

WILHELM, D. L., MILL, P. J., SPARROW, Elizabeth M., MACKAY, Margaret E. & MILES, A. A. **Enzyme-Like Globulins from Serum reproducing the Vascular Phenomena of Inflammation. IV. Activable Permeability Factor and its Inhibitor in the Serum of the Rat and the Rabbit.** *Brit. J. Exper. Path.* 1958, June, v. 39, No. 3, 228–50, 7 figs. [22 refs.]

Guineapig serum contains substances which cause increased capillary permeability (PF) in guineapig skin; in this serum is found also an inhibitor to the permeability factor (IPF). This paper gives an account of studies undertaken to determine whether similar PF-IPF systems exist in rat and rabbit serum, the activity being tested on the same animal as that from which the serum was obtained.

Undiluted rat serum has slight PF activity, especially when it is a few hours old. However, in serum which has been serially diluted and allowed to stand at room temperature for 1 hour there appears a PF (Dil) in the dilutions 1/45 to 1/135. This PF disappears and there is none present in dilutions which have stood for 4 hours at room temperature. These findings are broadly similar to the system in guineapigs. As in guineapigs an inhibitor IPF was found in rat serum, but because of technical difficulties it was not possible to demonstrate directly its action on rat PF (Dil).

Rat serum was fractionated by methods already described by WILHELM, MILL and MILES [this *Bulletin*, 1958, v. 33, 195]. Of the fractions, G2, consisting of alpha- and beta-globulins, carried most PF activity and in fact the PF activable from 1 ml. of rat serum by fractionation was 6 times greater than obtained by dilution, *i.e.* PF (Dil). PF/G2 is a large molecular substance and is either an alpha-globulin or intimately associated with it. Its activity in rat skin was to some extent inhibited by mepyramine maleate, suggesting that PF activity was due partly to a histamine liberator. Several appropriate biological systems were used but in

none was it possible to demonstrate PF/G2 as a histamine liberator.

Fractions containing alpha-globulin and albumins contained an inhibitor to PF/G2. It was not possible to determine whether the inhibitory activity was associated exclusively with either of these substances.

In the rabbit the main PF was, unlike that in guinea-pig or rat, in undiluted serum. This native PF (Nat) differed from PF (Dil) of rats and guineapigs in not being inhibited by soya bean trypsin inhibitor. The PF was inhibited by mepyramine injected locally. Fractionating rabbit serum a PF was obtained, PF/G2, which is thought to be a large molecular substance associated with the alpha- and beta-globulins. Increased permeability required about 2 hours to reach its maximum, in contrast with 2–3 minutes for guineapig and rat PF (Dil).

An inhibitor IPF was found in a fraction which consisted almost entirely of albumin.

Douglas D. Smith

ELDER, J. M. & WILHELM, D. L. **Enzyme-Like Globulins from Serum reproducing the Vascular Phenomena of Inflammation. V. Activable Permeability Factor in Human Serum.** *Brit. J. Exper. Path.* 1958, Aug., v. 39, No. 4, 335–42, 5 figs. [10 refs.]

Human serum has been examined for substances causing increased capillary permeability in the skin of guineapigs. Fresh undiluted serum contains a PF (Nat) similar to that found in fresh rabbit serum and in rat serum which has been allowed to stand for up to 1 hour.

When dilutions of human serum are made and tested for PF there is only that due to PF (Nat), but after standing for 1 day at 4°C. a secondary peak appears at 1/225 dilution. The new PF is analogous with the PF (Dil) of guineapig serum. There is also evidence that an inhibitor is present and active at the lower dilutions. PF (Dil) is heat-labile, is susceptible to soya bean trypsin inhibitor and guineapig IPF, but is not susceptible to mepyramine maleate.

By prolonged dialysis it is possible to remove the inhibitory effect of IPF against PF (Dil), suggesting that a dialysable substance is essential for the action of the inhibitor. *Douglas D. Smith*

MILL, P. J., ELDER, J. M., MILES, A. A. & WILHELM, D. L. **Enzyme-Like Globulins from Serum reproducing the Vascular Phenomena of Inflammation. VI. Isolation and Properties of Permeability Factor and its Inhibitor in Human Plasma.** *Brit. J. Exper. Path.* 1958, Aug., v. 39, No. 4, 343–55, 8 figs. [20 refs.]

In human plasma a potent capillary permeability factor was found associated with beta-globulin. The PF activity was measured on guineapig skin. PF obtained from ether fractionation by the standard method of KEKWICK and MACKAY [this *Bulletin*, 1955, v. 30, 190] was of low potency and a modified system is described which greatly increased the yield. The potency and behaviour of PF in fractions justify the assumption that it is identical with PF (Dil) and distinct from PF (Nat); it is also similar to PF (Dil) of guineapigs and rats. Tested in human skin by the scratch method, human PF (Dil) caused a weal but no flare such as is caused by histamine; the wealing was not inhibited by mepyramine maleate.

Plasmin was present in PF preparations but the two substances were shown to be distinct by virtue of the fact that PF was more heat-labile.

One of the fractions contained an IPF active against human but not against guineapig PF.

[These three articles contain much detailed information, which cannot be abstracted, regarding the technique of using laboratory animals for capillary permeability studies.] *Douglas D. Smith*

Miscellaneous

WORLD HEALTH ORGANIZATION. **Publications of the World Health Organization 1947–1957. A Bibliography.** 128 pp. 1958. Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office.] [17s. 6d.; $3.25; Sw. fr. 10.–.]

This publication contains references to articles which appeared from 1947 to the end of 1957 in the World Health Organization *Bulletin* (v. 1–17), *Chronicle* (v. 1–11), *International Digest of Health Legislation* (v. 1–8), *Epidemiological and Vital Statistics Report* (other than regularly recurring items) (v. 1–10), *Technical Reports Series* (Nos. 1–141), *Official Records* (Nos. 1–81), *Monograph Series* (Nos. 1–36), Supplements to the *Weekly Epidemiological Record* and occasional publications such as the *World Directory of Medical Schools*. It is arranged in 5 parts: technical articles and publications, in alphabetical order; administrative and general articles and publications, in alphabetical order; author index; index of countries; and list of publications by series. The languages of publication—normally English and French, but occasionally Chinese, Russian and Spanish —are indicated.

It is pointed out in the introduction that the bibliography does not include references to mimeographed documents which are issued in limited numbers by

WHO as working papers and are not available for general distribution. No mention is made, however, of the publications of the WHO Regional Offices which are obtainable by purchase or are distributed on a restricted basis to depository libraries or other appropriate institutions. This omission is to be regretted, since a bibliography of WHO publications might reasonably be expected to refer to the works of Regional Offices which form an integral part of the Organization.

This is, nevertheless, a valuable source of reference to articles and reports written by authors of international standing in the research, medical and public health fields. *A. H. Phipps*

PRIGGE, R. Bericht über die Tätigkeit der Staatlichen Anstalt für experimentelle Therapie Paul-Ehrlich-Institut, des Chemotherapeutischen Forschungsinstituts Georg-Speyer-Haus und des Ferdinand-Blum-Instituts für experimentelle Biologie zu Frankfurt a.M. in der Zeit vom 1. Januar 1952 bis 31. Dezember 1956. [**Report of the Activities of the Paul-Ehrlich State Institute for Experimental Therapy, the Georg-Speyer-Haus Chemotherapeutic Research Institute and the Ferdinand-Blum-Institute for Experimental Biology at Frankfurt a.M., for 1952 to 1956**] *Arb. a.d. Paul-Ehrlich-Inst. u.s.w. Frankfurt/M.* 1958, No. 55, pp. v + 129.

Book Reviews

TAYLOR, Edwin Windle [M.A., M.D., B.Ch., M.R.C.S., L.R.C.P., D.P.H.] [Revised by]. **The Examination of Waters and Water Supplies** [THRESH, BEALE & SUCKLING]. 7th Edition. pp. viii + 841, 51 illustrations. 1958. London: J. & A. Churchill Ltd., 104, Gloucester Place, W.1. [£5.]

This is the second edition of "Thresh, Beale and Suckling" for which Dr. Windle Taylor has been responsible. The revision has plainly been thorough, for a glance at the lists of references shows that in almost every chapter material published during the 9 years since the last edition appeared has been incorporated. Important developments have occurred during this period in many of the fields covered, including the nomenclature of the *coli-aerogenes* bacteria, the use of membrane-filtration technique in bacteriological examination, the extension of complexometric methods of chemical analysis, and many others. Revised editions of standard books on methods of analysis of water and sewage have appeared during the last few years, both in Great Britain and the United States, and a considerable amount of new material from these sources has been incorporated in the book under review.

The general arrangement of the subject matter follows that of the sixth edition [this *Bulletin*, 1950, v. 25, 84], but there has been a little rearrangement, mainly with the object of reducing repetition, and some new chapters have been added.

One of these new chapters is concerned with radioactivity in water, a new hazard for the supplier of water. The author first considers the nature of radioactivity, its natural and artificial sources and its danger to man, and then describes methods for determining the radio-activity of samples of water and of some other materials, such as the sand in filter beds, and discusses methods for disposing of radio-active materials. The removal of radio-activity from contaminated water is also dealt with, but it is pointed out that most of the work on this subject has been on a laboratory scale only, and that the results show that only a small proportion of the activity can be removed by normal water-treatment processes.

Another type of pollution which has become widespread since the publication of the last edition of this book is that due to synthetic detergents. A large proportion of these materials has been passing unchanged through sewage-treatment plants and has consequently reached streams which are sources of public supply. A method for estimating these materials is now included in the chapter on the examination of grossly polluted water, sewage and sewage effluents.

A welcome change is the inclusion of excellent photographs of plant and animal aquatic organisms in place of the line drawings used in the last edition; it should be much easier to relate these to the organisms seen under the microscope. *N. H. Johnson*

RHODES, A. J. [M.D., F.R.C.P., F.R.S.C.,] & VAN ROOYEN, C. E. [M.D., D.Sc., M.R.C.P., F.R.C.P.] **Textbook of Virology for Students and Practitioners of Medicine.** 3rd Edition. pp. xv + 642, 81 figs. 1958. London: Baillière, Tindall & Cox Ltd., 7 & 8, Henrietta Street, W.C.2. [80s.]

The extensive development of virology in the last few years has rendered all text-books out of date, and it is thus of particular value to have a new edition of this popular work, which is published in the current year and contains material up to and including 1957. There has been no change in style and layout, and the book is still classified on traditional lines into sections on skin diseases, exanthemata, respiratory diseases and so on. It still includes a section on rickettsial diseases, although these organisms are now definitely out of place in a text-book of virology. The section is nevertheless a useful reference account, but the article on trench fever is still based mainly on information acquired during the 1914–18 war. The agents of the psittacosis-lymphogranuloma group are still included, albeit scattered over 3 chapters; it is traditional to

include them in works on virology, although many authorities now consider that they are rickettsiae. The increase of knowledge has necessitated expansion of the section on Coxsackie viruses; a subsection on adenoviruses is now included in the section on respiratory diseases; and cytomegalic inclusion disease also receives a mention. The section on skin diseases is little changed, and a comparison with the previous edition accurately reflects the unpopularity of warts, molluscum and shingles among contemporary investigators. The account of poliomyelitis is enlarged to include an account of vaccine trials up to 1955, but it would have been of interest to have learnt a little more about B virus infection, which is an important problem in the production of poliomyelitis vaccine.

The work makes no claims to being a monograph and is clearly not intended for the professional virologist, but it can be confidently recommended to undergraduate and postgraduate students who wish to have a reliable and reasonably up-to-date account of the present state of knowledge of virology.

D. J. Bauer

DRUMMOND, J. C. & WILBRAHAM, Anne. **The Englishman's Food. A History of Five Centuries of English Diet.** Revised, and with a New Chapter by Dorothy HOLLINGSWORTH, and a Preface by Norman C. WRIGHT, C.B., D.Sc. 482 pp., 8 pls. 1957. London: Jonathan Cape Ltd., 30, Bedford Square, W.C.1 [36s.]

There are histories of the science of nutrition, and there are histories of the art of cookery. Until 1939 there was no scientific account of English food. The Rev. Richard WARNER had in 1791 published an admirably documented account of English meals from the earliest times, but until the present century no attempt was possible to relate the Englishman's food at different periods to his nutritional requirements. When in 1939 Sir Jack and the future Lady Drummond attempted this, quantitative nutritional requirements were beginning to be available. In a book which quickly went out of print they traced changes in diet from medieval times until the late thirties of the present century, in the food grown and imported, in the distribution and marketing of food and in its effect on health.

They gave a valuable account of the strategic importance of nutrition in the First World War. Their book was published just before the Second World War, during which nutrition played an even greater part. Not only was deterioration in health from war-time shortages prevented, but active steps were taken to improve the health of the people.

These great advances in the application of nutritional science, together with the rapid advances in the science itself, have made a new edition essential. This need has been admirably fulfilled by Miss Dorothy Hollingsworth, who was closely associated with Sir Jack at the Ministry of Food. She has revised the account of 5 centuries of British diet to bring it into line with current knowledge, and has shortened it by omission of unnecessary references and illustrations. The last 2 chapters have been replaced by a new one in which Miss Hollingsworth has made an admirable survey of the 2 World Wars and the peace-time application in Britain of the science of nutrition.

This excellent book combines the scientific knowledge of nutrition with the sociological implications of changes in diet, and provides a clear authoritative account of the Englishman's food through the ages. *H. M. Sinclair*

HALLAUER, C. & MEYER, K. F. [Edited by.] Handbuch der Virusforschung [**Handbook of Virus Research**] Vol. IV., pp. xv + 688, 61 figs. 1958. Vienna 1: Springer-Verlag, Mölkerbastei 5. [£12.11.6]

The previous volumes and parts of this work appeared in 1938, 1939, 1944 and 1950 under the editorship of DOERR and HALLAUER, and the first 3 are now out of print. The present volume continues the monographic style of its precursors, and is divided into a general and a special part, of more or less equal length.

The general part contains sections on the genetics of animal viruses (F. M. BURNET) and phages (P. FREDERICQ, in French), a survey of insect viruses (G. H. BERGOLD), arthropods as vectors of plant viruses (K. M. SMITH) and animal viruses (W. C. REEVES), and the use of tissue cultures for the isolation of viruses (W. KLÖNE, in German).

The special part contains sections on encephalitis viruses (P. LEPINE, P. GOUBE DE LAFOREST, in French), foot-and-mouth disease virus (H. RÖHRER and G. PYL, in German), the EMC group of viruses (C. W. JUNGEBLUT), poliomyelitis viruses (S. GARD), and the Coxsackie viruses (H. LÖFFLER, in German). Each section has thus been entrusted to an acknowledged authority on the subject concerned, who has attempted to produce a comprehensive monograph within the space allowed, but here the fundamental weakness of a handbook of this type is immediately apparent. Virology is expanding far too rapidly to be restricted to such rigid confines. The section on Coxsackie viruses, for example, although it has a bibliography of 272 references, has been severely compressed to fit it into 24 pages. What is needed is rather a series of separately published monographs, each devoted to a particular virus or group of viruses, appearing as and when necessitated by the growth of the subject, published in the shortest possible time after the appearance of the last work which is included, and kept up-to-date by the appearance of supplementary volumes until new editions become necessary. To say this is not to decry in any way the energy and industry of the editors and contributors to the present work, but is merely a statement of the evident fact that a Handbook in the tradition of Teutonic scholarship does not become justifiable until the development of its subject has begun to lose its impetus. *D. J. Bauer*

OSWALD, Neville C. [T.D., M.D., F.R.C.P.] [Edited by.] **Recent Trends in Chronic Bronchitis.** pp. vii + 199, 74 figs. 1958. London: Lloyd-Luke (Medical Books) Ltd., 49, Newman Street, W.1. [30s.]

Chronic bronchitis is a disease in which research is difficult: consequently from about the turn of the century until the last war little progress was made in

elucidating its pathology. In the early stages the symptoms are slight and pathological material is seldom available, and in the late stages the secondary changes make the material useless. Again, the condition is confined largely to countries with a cold and damp climate, and has been called "the English disease", and therefore little research has been done abroad. Recently much more work has been done on the subject. This volume contains a series of essays on various aspects of chronic bronchitis by workers in their own fields, mainly drawn from the Brompton and St. Bartholomew's hospitals, London. The reader is provided with the results of the latest research, written in clear language.

The monograph starts with an admirable survey by Neville C. OSWALD in which the problems are clearly stated, and above all the terminology is defined, saving much confusion. All the succeeding papers are of a high standard, and by collecting in a small volume the results of work widely scattered in the medical literature a broad view of the subject is given. It is difficult to select papers for special mention, but the reviewer was particularly interested in those by Lynne REID (Pathology), Ronald GIBSON (The Heart in Chronic Bronchitis and Emphysema), and Neville Oswald (Mucus). All papers have up-to-date bibliographies.

Unlike so many volumes with a number of contributors, excellent editing has prevented overlapping. N. C. Oswald and his colleagues are to be congratulated on this work. If the reviewer tries to find something to criticize it may be the title, which underestimates the scope of the book, but obviously the editor feels that the subject is still too nebulous to allow him to give it a more imposing title. No one interested in diseases of the chest can afford to miss reading this book. *F. H. Young*

MEIKLEJOHN, A. [M.D.] **The Life, Work and Times of Charles Turner Thackrah, Surgeon and Apothecary of Leeds (1795–1833),** pp. vii + 238, 7 figs. on 7 pls. 1957. Edinburgh. London: E. & S. Livingstone Ltd. [25s.]

The main part of this work consists of a photolithographic facsimile of the second edition of Thackrah's book *The effects of arts, trades, and professions, and of civic states and habits of living, on health and longevity,* [etc.], published in 1832, and we are fortunate that this classic work is once more made available. Dr. Meiklejohn's biographical essay is the result of a thorough investigation into original sources, and corrects several errors that have appeared in previous biographical memoirs.

Charles Turner Thackrah was born in Leeds on May 22, 1795, the son of a chemist, which possibly influenced his becoming apprenticed to a surgeon and apothecary at the age of 16. Upon completing his apprenticeship in 1815, Thackrah entered Guy's Hospital as a pupil, coming under the influence of Astley Cooper. Qualifying as an apothecary and a member of the College of Surgeons in 1816, Thackrah returned to Leeds, but suffered severely from ill-health. He conducted some experiments on the blood, for which he won a prize offered by Astley Cooper, and reported on lodging houses at the request of the Leeds Workhouse Board. Thackrah entered into partnership with his former master at Leeds, and acted as joint secretary of the Leeds Philosophical and Literary Society. He established a school of anatomy which was merged in the Leeds School of Medicine.

Charles Thackrah had ample opportunity to study social conditions in a factory town, and he was particularly interested in preventive medicine. His book on the subject was first published in 1831, when he was already suffering from tuberculosis. It was reprinted in Philadelphia, and his reputation was high on both sides of the Atlantic. He investigated an epidemic of cholera on Tyneside and published a tract on the subject. His earlier book rapidly sold out, and the text was thoroughly revised for the second edition. Unfortunately the author died on May 23, 1833, at the age of 38. The Leeds Medical School remembers Thackrah as its founder, but it is suggested that his real claim to fame is this book. *John R. Brown*

KEEVIL, J. J. **Medicine and the Navy 1200–1900. Vol. I. 1200–1694.** Introduction by Henry DALE. pp. xii + 255, frontispiece, 1 folding plan & 13 figs. on 13 pls. 1957. Edinburgh. London: E. & S. Livingstone Ltd. [40s.]

The history of naval medicine is a most fascinating topic, but has not heretofore been the subject of systematic study. It demands the combination of a medical historian with a keen knowledge of naval affairs, and in Commander Keevil the ideal person was found. Aided by the Wellcome Trustees he spent several years investigating original sources; the Public Record Office, museums, libraries and hospitals were scoured for both manuscript records and printed material. The resultant accumulation has been carefully digested, and the first volume, covering the years 1200–1694, presents a well documented study of the subject.

This is more than a history of medicine in the navy; it traces the development of the navy itself, for this has depended largely upon the health of the sailors. We encounter familiar names in John Woodall, James Yonge, William Clowes and Thomas Gale, among others, to remind us that through their writings naval surgeons influenced the development of their craft in general. But this book also records less well-known figures, and expeditions to remote parts of the globe. Scurvy featured prominently among the scourges of seamen; medicine chests were of vital importance. These are adequately considered in a comprehensive study that is an example to all historians. An encyclopaedic work, with adequate references, and a chronology of important events. *John R. Brown*

Printed in Great Britain by The Eastern Press, Ltd., London and Reading.